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PART ONE

KINETICS OF THE DEUTERIUM EXCHANGE OF SUBSTITUTED METHYL ACETATES

PART TWO

EQUILIBRIUM IN THE ISOMERIZATION OF CERTAIN UNSATURATED COMPOUNDS

A THESIS

Presented to

the Faculty of the Graduate Division

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PART ONE

KINETICS OF THE DEUTERIUM EXCHANGE OF SUBSTITUTED METHYL ACETATES

PART TWO

EQUILIBRIUM IN THE ISOMERIZATION OF CERTAIN UNSATURATED COMPOUNDS

Approved:

Chairman

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SUMMARY

PART ONE

According to the Pauling equation defining electronegativity the energy of a carbon-X bond in a saturated compound can be expressed as

$$BE_{C-X} = 1/2\ (BE_{C-C} + BE_{X-X}) + 23(X_X - X_C)^2$$

where BE's are the bond energies (in kcal/mole) of the bonds denoted by subscripts and X's are electronegativities. If the electronegativity of carbon stand in the order $C_{sp} > C_{sp}2 > C_{sp}3$ as has been reported, the C-X bond energy should be affected by the hybridization of this carbon in such a way that when X is highly electronegative the bond energies should stand in the order $C_{sp}3\text{-}X > C_{sp}2\text{-}X > C_{sp}\text{-}X$. There are data that suggests that fluoroolefins are less stable than their saturated analogues, however, there are other factors which complicate interpretation of this data.

The energetics of reactions involving a change in the hybridization of a carbon atom bound to X should be affected by the electronegativity of X. Thus ΔH_X for the transformation of $C_{sp}3\text{-}X$ to $C_{sp}2\text{-}X$ should contain a term due to the enthalpy of rehybridization.

$$BE_{C_{sp}2\text{-}X} - BE_{C_{sp}3\text{-}X} = 1/2\ (BE_{C_{sp}2\text{-}C_{sp}2} - BE_{C_{sp}3\text{-}C_{sp}3})$$
$$+ 23(X_{C_{sp}2}{}^2 - 2X_{C_{sp}2}X_X - X_{C_{sp}3}{}^2 + 2X_{C_{sp}3}X_X)$$

If the same transformation is considered in which X is replaced by Y, an analogous equation can be written; furthermore, the difference, $\Delta H_X - \Delta H_Y$, is simply stated in terms of the differences in electronegativity $X_Y - X_X$ and $X_{Csp^2} - X_{Csp^3}$.

$$\Delta H_X - \Delta H_Y = -46(X_{Csp^2} - X_{Csp^3})(X_X - X_Y)$$

In as far as entropy changes are independent of the nature of the substituents, $\Delta\Delta H = \Delta\Delta F$, and this equation becomes a <u>linear free energy relationship</u> which may be applied to equilibria and kinetic processes.

$$\log \frac{K_X}{K_Y} = \rho^H \sigma^H$$

$$\text{where: } \rho^H = \frac{46}{2.3RT}(X_{Csp^2} - X_{Csp^3}); \; \sigma^H = X_X - X_Y$$

$$\log \frac{k_X}{k_Y} = \rho^H \sigma^H$$

The latter equation applies to kinetic processes and X_{Csp^2} must necessarily refer to the hybridization of carbon attained in the transition state (in some reactions this will be very nearly sp^2).

This equation may be applied to a reaction of the type

$$XYCHCO_2CH_3 + B^- \rightleftharpoons XY\bar{C}CO_2CH_3 + BH$$

since the formation of the carbanion is almost surely accompanied by a

change in the hybridization of the alpha carbon from sp^3 to sp^2. Therefore, we have measured the kinetics of the deuterium exchange of alpha substituted methyl acetates in methanol-O-d using sodium methoxide as catalyst in order to test this relationship. The rates were followed at 35^o by infrared measurements at 3360 cm^{-1} where the protiomethanol formed in the reaction absorbs strongly. The observed second-order rate constants for the attack of methoxide upon alpha hydrogen were calculated using an equation for simple pseudo first-order kinetics. This procedure ignores primary and secondary kinetic isotope effects (which are thought

$$k[CH_3ONa]t = 2.303 \log \frac{[CH_3OH]_\infty - [CH_3OH]_o}{[CH_3OH]_\infty - [CH_3OH]}$$

to be small enough to be neglected) and as such gives a reasonable measure of the relative rates of carbanion formation.

The data were correlated in terms of a two-mechanism interaction in which polar effects and hybridization effects are considered.

$$\log \frac{k}{k_o} = \rho^*(\sigma_X^* + \sigma_Y^*) + \rho^H(X_X + X_Y - 2X_o)$$

A Taft correlation of the form

$$\log k + \rho^*(\sigma_X^* + \sigma_Y^*) + \log k_o$$

where ρ^* is 1.79 and $\log k_o$ is 4.604 was established for five compounds

with an average deviation of 0.04 log units. However, fluoroacetate, methoxyacetate, dimethoxyacetate, and difluoroacetate showed significant negative deviations (corresponding to low reactivity). The deviation from the Taft plot for the monosubstituted acetates, dimethoxyacetate, and acetate are reasonably correlated (± 0.4 log units) in terms of ρ^H $(X_X + X_Y - 2X_C)$ where ρ^H is - 2.4. This value of ρ^H corresponds to a value of $X_{Xsp^2} - X_{Csp^3}$ equal to 0.073 electronegativity units which is consistent with another estimate reported. Difluoroacetate is found to be in reasonable agreement with this correlation when a correction is made for double bond - no bond resonance in the ester; however, when such a correction is made for dimethoxyacetate it appears to be more reactive than predicted by about three powers of ten. It was suggested that alkoxy oxygens might stabilize the transition state by resonance donation of their unshared pairs of electrons to the pi system of the incipient enolate anion. Thus, this correlation accounts for apparent deviations from the Taft equation which are as large as four powers of ten and perhaps as great as eight powers of ten.

SUMMARY

PART TWO

The postulate, offered in part one, that highly electronegative groups tend to destabilize olefins is examined in this work in terms of the effect of methoxy and thiomethoxy groups upon the stability of certain unsaturated compounds. The relative stabilities of various isomeric methoxy and/or thiomethoxy substituted unsaturated compounds were determined by base-catalyzed isomerization reactions.

The results are presented in the table and were obtained using nuclear magnetic spectroscopy as the analytical method. The isomerization of 1,1-dimethoxypropene and 3,3-dimethoxypropene was attempted without success. The isomerization of 1-methoxy-4-methythio-2-butene was attempted but elimination of methanol was found to take place at a rate comparable to the rate of isomerization.

Entries 1 and 2 in the table (trans-isomers) show that methoxy groups stabilize olefins more than thiomethoxy groups do by about 2.2 kcal/mole. Any destabilization of the olefin by the more electronegative methoxy group appears to be offset by the greater ability of oxygen than sulfur to stabilize the olefin by resonance conjugation of its unshared electron pairs with the pi system of the double bond. Entries 3, 4, 5, and 6 also can be compared to give a value of 2.06 kcal/mole for the greater stabilization of olefins by a methoxy group.

Compound	T°	Solvent	Mole per cent at Equilibrium cis	trans
$CH_3OCH_2CH{=}CHSCH_3$	50°	DMSO	ca. 1	ca. 2[a]
$CH_3OCH{=}CHCH_2SCH_3$	50°	DMSO	31.6	65.5
$CH_3OCH_2CH{=}CHCO_2CH_3$	35°	tert-BuOH	—[b]	2.02[a]
$CH_3OCH{=}CHCH_2CO_2CH_3$	35°	tert-BuOH	98[a]	—[c]
$CH_3SCH_2CH{=}CHCO_2CH_3$	35°	tert-BuOH	—[b]	42.3
$CH_3SCH{=}CHCH_2CO_2CH_3$	35°	tert-BuOH	23.9	33.8
$CH_3OCH_2C{\equiv}CH$	ca. 25°	DMSO	ca. 1[a]	
$CH_3OCH{=}C{=}CH_2$	ca. 25°	DMSO	99	
$CH_3OC{\equiv}CCH_3$	ca. 25°	DMSO	—[c]	

[a] Equilibrium values in as far as a steady state was attained.

[b] Thought to be too unstable to detect.

[c] Not formed due to kinetic control.

Entries 3 through 6 have been shown to be in reasonable agreement to what might be predicted from other data in the literature. The data available do not offer any support for the operation of the hybridization effect.

PART ONE

CHAPTER I

INTRODUCTION

Pauling (1) has correlated the excess energy of an A-B bond above the mean energy of the A-A and B-B bonds with the difference in electronegativity between atoms A and B. Pauling's scale of electronegativity is, in fact, based upon a best fit of bond energies to the equation

$$BE_{A-B} = \frac{1}{2}(BE_{A-A} + BE_{B-B}) + 23(X_A - X_B)^2 \qquad (1)$$

if the arithmetric mean is used, or

$$BE_{A-B} = \sqrt{(BE_{A-A})(BE_{B-B})} + 23(X_A - X_B)^2 \qquad (2)$$

if the geometric mean is used. The electronegativity scale thus obtained has been compared with electronegativity scales derived in other ways, such as from electron affinities and ionization potentials, Hammett and/or Taft substituent constants, and dipole moments (2, 3). Pauling rationalized the excess bond energy of an A-B bond in terms of ionic resonance

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1. L. Pauling, "The Nature of the Chemical Bond," 3rd ed., Cornell University Press, Ithaca, New York, 1960, pp. 85-105.

2. H. O. Pritchard and H. A. Skinner, Chem. Rev., 55, 745 (1955).

3. R. W. Taft, Jr., J. Chem. Phys., 26, 93 (1957).

contributions of the type:

$$A-B \longleftrightarrow A^{+}\ B^{-}$$

where B is the more electronegative atom.

There is a large amount of evidence that the electronegativity of carbon depends on its state of hybridization. Electronegativity of carbon is found to increase as its s-character of hybridization is increased, such that the sp-hybrid is more electronegative than the sp^2-hybrid which is in turn more electronegative than the sp^3-hybrid (4). This variation in the electronegativity of carbon should affect the strengths of bonds to carbon and this should be more pronounced with bound atoms of high electronegativity. Such a contribution to bond strengths should be observable in transformations in which a bound carbon undergoes a change in its state of hybridization. Consider, for example, the generalized transformation in which a carbon atom undergoes a change in hybridization from sp^3 to sp^2. The specific energy effect, or "Hybridization Effect," re-

$$-\overset{|}{\underset{|}{C}}-Y \longrightarrow =\overset{|}{C}-Y$$

sulting from the change in the C-Y bond energy can be expressed in terms

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4. G. W. Wheland, "Resonance in Organic Chemistry," John Wiley and Sons, Inc., New York, 1955, pp. 128, 221, 350.

of equation number 1, where the subscripts 2 and 3 refer to $\underline{sp}^2$ and $\underline{sp}^3$

$$-\Delta H_Y = \tfrac{1}{2}(BE_{22} + BE_{Y-Y}) + 23(X_Y - X_2)^2 - \tfrac{1}{2}(BE_{33} + BE_{Y-Y}) - 23(X_Y - X_3)^2 \qquad (3)$$

carbon respectively. This equation can be written as:

$$-\Delta H_Y = \tfrac{1}{2}(BE_{22} - BE_{33}) - 46D(X_Y - X_3) + 23D^2 \qquad (4)$$

$$\text{where } D = X_2 - X_3$$

Thus ΔH_Y is that portion of the overall enthalpy change of reaction which is due to the hybridization effect. This effect may be further isolated by considering the same transformation in which Y is replaced by atom Z.

$$-\Delta H_Z = \tfrac{1}{2}(BE_{22} - BE_{33}) - 46D(X_Z - X_3) + 23D^2 \qquad (5)$$

On comparing the two reactions, by using equations 4 and 5, we obtain:

$$\Delta H_Y - \Delta H_Z = 46D(X_Y - X_Z) \qquad (6)$$

If the entropy change, ΔS, is assumed to be independent of the nature of Y and Z, the difference in enthalpy, $\Delta H_Y - \Delta H_Z$, can be replaced by the difference in free energies, $\Delta F_Y - \Delta F_Z$.

$$\Delta F_Y - \Delta F_Z = 46D(X_Y - X_Z) \qquad (7)$$

ɪation effect is now expressed in terms of a simple linear free tionship, in which the equilibrium constant can be expressed as:

$$\log \frac{K_Y}{K_Z} = \rho^H \sigma^H + G(Y,Z)$$

$$\rho^H = \frac{46D}{2.3RT} \quad ; \quad \sigma^H = \mathbf{X}_Y - X_Z \tag{8}$$

Y,Z) is some function which expresses the free energy changes er interaction mechanisms of the substituent groups Y and Z with the molecule.

he elucidation of the effect of substituents on reactivity, po- nce, and steric effects are recognized as major factors. Polar e been correlated with good success for many systems using the relations of Hammett and Taft. Resonance effects are treated ent in the Hammett relation, but resonance and steric effects in not capable at present of general correlation. Proper choice systems can, however, minimize these effects or at least hold ially constant for a given set of substituents.

tions involving substituents attached to carbon undergoing a ybridization might be expected, where resonance and steric constant, to conform to the relations:

$$\log \frac{K}{K_o} = \rho^* \sigma^* + \rho^H \sigma^H \tag{9}$$

$$\log \frac{k}{k_o} = \rho^* \sigma^* + \rho^H \sigma^H \tag{10}$$

where $\rho^* \sigma^*$ gives the polar effect upon the equilibrium or rate, according to the Taft relation, and where $\rho^H \sigma^H$ accounts for the hybridization effect. The value of ρ^H would be dependent upon the rehybridization attained in the product or transition state.

An estimation of the expected magnitude of the hybridization effect can be gotten from the data of Gordy (5) who estimates sp carbon to be 0.28 units more electronegative than sp^3 carbon. If it is estimated that sp^2 carbon is 0.10 units more electronegative than sp^3 carbon, then 8.7 kcal/mole should be the decrease in free energy of reaction for rehybridization, sp^2 to sp^3, of carbon bound to fluorine compared with the same carbon bound to hydrogen. Such effects as resonance interaction of the carbon bound atom with the multiple bond of carbon have been ignored here. The inclusion of these effects operate energetically in such a way as to oppose, in the case of fluorine, the hybridization effect. Note that for the case of oxygen as a substituent the hybridization effect should be smaller and the resonance with the double bond would certainly be greater.

Patrick (6, 7) has compiled data which suggest that olefins containing fluorine attached to double bonds are less stable than their saturated analogues, and explains this in terms of a weakening of the double bond. The relative instability of the fluoro-olefins may be due, in part,

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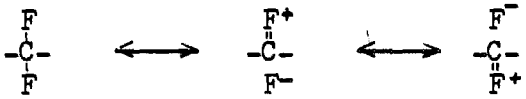
5. W. Gordy, J. Chem. Phys., 14, 305 (1946).

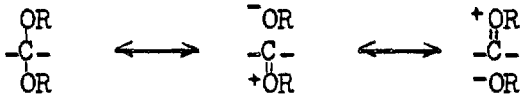
6. C. R. Patrick, Tetrahedron, 4, 26 (1958).

7. C. R. Patrick, "Advances in Fluorine Chemistry," Vol. 2, Butterworth's, Washington, 1961, Chap., 1.

to the hybridization effect, but it appears that the greater part is due to stabilization of the saturated analogues. Hine (8) correlated a large amount of data on the stability of saturated polyfluoro compounds in terms of double bond - no bond resonance. This resonance involves fluorine atoms which are attached to the same saturated carbon atom and is estimated to give roughly 3.2 kcal/mole of stabilization for each double bond - no bond resonance structure involving fluorine atoms (or 6.5 kcal/mole for each fluorine-fluorine interaction).



A similar resonance in alkoxy compounds results in a stabilization of approximately 3.5 kcal/mole per resonance structure.



As a case in point, the polymerization of tetrafluoroethylene is about 16 kcal/mole more exothermic than of ethylene (7).

$$CF_2{=}CF_2 \longrightarrow 1/n(-CF_2-CF_2-)n \qquad \Delta H = -42 \text{ kcal/mole}$$

$$\Delta S = -45 \text{ eu}$$

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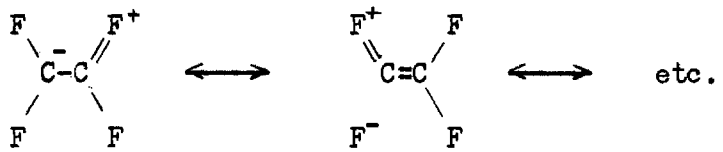
8. J. Hine, J. Am. Chem. Soc., 85, 3239 (1963).

$$CH_2{=}CH_2 \longrightarrow 1/n(-CH_2-CH_2-)n \qquad \Delta H = -24.7 \text{ kcal/mole}$$
$$\Delta S = -37 \text{ eu}$$

The extra stabilization of polyfluoroethylene due to double bond - no bond resonance accounts for roughly 13 kcal/mole of the 16 kcal/mole difference in heats of polymerization and it is possible that the hybridization effect is responsible for the extra 3 kcal/mole. Although this value is too small and uncertain to be useful, it presumably should be made larger by an amount equal to the resonance stabilization of tetrafluoroethylene by structures such as:



Unfortunately, it is not possible to estimate the effect of such resonance at present.

Other evidence comes from the work of Kumler and co-workers (9) who used n.m.r. measurements to study the extent of enolization of oxaloacetic acid, diethyl oxaloacetate, and diethyl fluorooxaloacetate. The acid was found to be 8 per cent enolized in water and 21 per cent enolized in methanol. Diethyl oxaloacetate was 50 per cent enolized in methanol and 79 per cent enolized in the pure liquid form. On the other hand, in

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9. W. D. Kumler, E. Kun, and J. N. Shoolery, J. Org. Chem., 27, 1165 (1962).

the pure liquid form, diethyl fluorooxaloacetate gave no detectable enol. If, "no enol" means less than 3 per cent enol, then introduction of the fluoro substituent has reduced the equilibrium constant for enolization by more than 120-fold. Introduction of bromine as substituent reduced the equilibrium constant by less than two fold (10).

Alkoxy groups appear to stabilize double bonds by resonance conjugation of the oxygen's unshared p electrons with the double bond (11) and in known cases this effect overshadows possible destabilization due to the electronegativity effect. A discussion of this subject as related to equilibria will be deferred to the second part of this thesis. This resonance interaction of oxygen and fluorine with a double bond is expected to be less important when the double bond is conjugated with electron rich centers.

Dinitromethane has a pK_A of 3.60 in water at 20° while dinitrofluoromethane has a pK_A of 7.70 under the same conditions (12). Surprisingly, the acidity of dinitromethane is reduced by a factor of $10^{4.1}$ upon introducing the fluoro substituent (this factor is $10^{3.8}$ if a statistical correction is made). The inductive effect of fluorine might have been expected to increase the acidity of dinitrofluoromethane by a factor of

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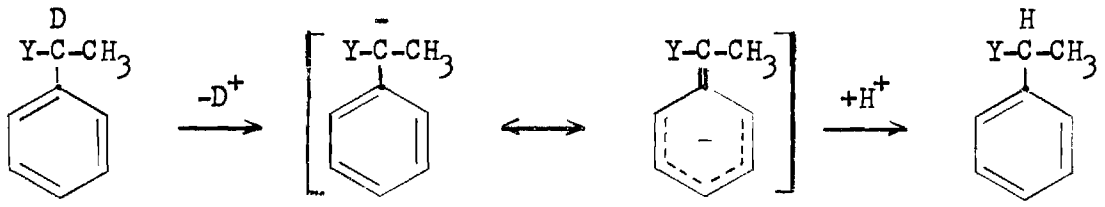
10. G. Schwarzenbach and E. Felder, Helv. Chim. Acta, 27, 1044 (1944).

11. G. W. Wheland, "Resonance in Organic Chemistry", John Wiley and Sons, Inc., New York, 1955, p. 85.

12. V. I. Slovetsky, L. V. Okholbstina, A. A. Fainzilberg, A. I. Ivanov, L. I. Biryukova, S. S. Novidov, Izv. Akad. Nauk SSSR, Otd. Khim. Nauk, 2063 (1965).

about 10^2 as observed in the case of acetic and fluoroacetic acid (in which the negative charge of the anion is separated from the fluoro substituent by two atoms). Cram and co-workers (13) have found that potassium tert-butoxide in dimethyl sulfoxide recemizes 1-methoxy-1-phenylethane-1-d about 1.4 times faster than 2-phenylbutane-2-d. It seems plausible that the transition state has much of the character of a benzylic carbanion since it was found that recemization accompanies deuterium exchange, for both within probable experimental error. The



Y = Et, OMe. Me, H

electron withdrawing power of the methoxy substituent (σ^* = ca. 1.8) is not much more effective than an ethyl substituent (σ^* = -0.10) in promoting alpha proton removal. Using this data the Taft ρ^* is only +0.077. In the same solvent, other workers (14) found that substitution of hydrogen for a methyl group in cumene gives a ten-fold increase in the rate (per hydrogen atom) of potassium tert-butoxide catalyzed alpha hydrogen exchange, which corresponds to a Taft ρ^* of about +2.0. This value can be used to predict a rate for the methoxy compound. If steric effects

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13. D. J. Cram, C. A. Kingsbury, and B. Rickborn, J. Am. Chem. Soc., 83, 3688 (1961).

14. J. E. Hofmann, R. J. Muller, and A. Schriesheim, ibid., 85, 3002 (1963).

do not greatly change the reactivity order, the methoxy compound is $10^{3.6}$ less reactive than what might have been predicted by polar effects alone. Using these data and Equations 8, 9, and 10, the difference in electronegativity of sp^2 carbon and sp^3 carbon, D, is estimated to be about 0.09 for the ionization of dinitromethane and 0.11 for formation of benzylic carbanions.

Additional data on the ionization of alpha fluoronitroalkanes also show that the fluoro substituent decreases the acidity of nitroalkanes. Adolph, Oesterling, and Kamlet have found that the ionization constants of ethyl nitroacetate, 2-nitroacetamide, and chloronitromethane are all decreased by the introduction of an alpha fluoro substituent although they are all increased by the introduction of alpha chlorine (15). The increases in pK_A (per alpha hydrogen) brought about by the fluorine substituent were 0.23, 0.41, and 2.64, respectively.

Cram and Lorand's report (16) that each of the four non-ring hydrogens of m-methylbenzal fluoride undergoes potassium tert-butoxide catalyzed deuterium exchange with tert-butyl alcohol-O-d at comparable rates can hardly be rationalized by a consideration of inductive effects alone. Cram's explanation in terms of the large p-character of the carbon-fluorine bond is related to the reason why sp^2 carbon is more electronegative than sp^3 carbon. It seems certain that double bond - no bond resonance stabilization of the benzal fluoride relative to the

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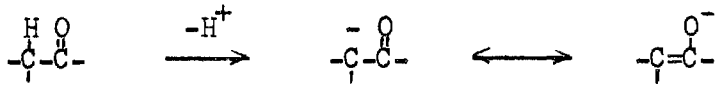
15. M. J. Kamlet, H. Adolph, and R. E. Oesterling,"Abstracts of Papers, 3rd International Symposium on Fluorine Chemistry," Munich, Germany, 1965, p. 242.

16. D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press, New York, 1965, p. 59.

transition state for removal of benzal hydrogen is responsible for part of the relatively low reactivity of this hydrogen.

The base catalyzed halogenation of ketones has been extensively studied and it appears certain that the rate controlling step is the removal of a proton alpha to the carbonyl group to produce a planar, resonance stabilized, enolate anion (17).



This system is of interest in that resonance donation of electrons, by groups attached to the alpha carbon, cannot effectively stabilize the enolate anion. Such resonance involves structures in which both the carbonyl carbon and the carbonyl oxygen bear negative

charge. Further, the stability of the enolate anion assures a large amount of enolate anion character to the transition state leading to its formation, hence the nature of the transition state is better defined. The hybridization of the alpha carbon in the transition state is assumed to be nearly sp^2, the negative charge residing largely on the more electronegative oxygen atom.

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17. J. Hine, "Physical Organic Chemistry," 2nd ed., McGraw-Hill Book Publishing Co., New York, 1962, p. 233.

Esters having hydrogen atoms alpha to the carbonyl group are also subject to electrophylic attack by bases to produce a resonance stabilized enolate anion. Cram has found that tert-butyl 2-phenylpropionate undergoes potassium tert-butoxide catalyzed deuterium exchange in tert-butanol at a rate equal to its racemization (18). This compound is considered to be converted to the enolate anion in which the charge of the carbanion is concentrated largely on oxygen. Racemization is thus assured by the intermediacy of the planar enol form. The purpose of this investigation is to examine the methoxide ion catalyzed deuterium exchange of certain alpha substituted methyl acetates and to use these data as a test for the operation of rehybridization effects.

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18. D. J. Cram, B. Rickborn, C. A. Kingsbury, and P. Harberfield, J. Am. Chem. Soc., 83, 3678 (1961).

CHAPTER II

EXPERIMENTAL RESULTS

Chemicals[1]

Benzene. Baker analyzed reagent grade product was used without further purification. Practical grade benzene, which had been distilled, served equally well.

Carbon Tetrachloride. Baker analyzed reagent grade product was used without further purification.

Dimethyl Succinate. A sample prepared from succinyl chloride by C. L. Liotta was fractionally frozen and the last solid portion obtained on melting was used.

Methyl Difluoroacetate. Columbia Chemical Company product was redistilled and processed on an Autoprep A-70 gas-liquid chromatography[2] instrument using a PDEAS column. Analysis of the neat liquid using n.m.r. and g.l.c. showed no detectible impurity.

Methyl Dimethoxyacetate. Eastman yellow label product was distilled on column number 1.

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[1] The boiling points that were determined are listed in Table 1 at the end of this section. See Instrumentation section for a discussion of apparatus.

[2] In following discussions the abbreviation g.l.c. will be used.

Methyl 3-Methoxypropionate. Aldrich Chemical Company product was distilled on column number 1.

Methyl Phenylacetate. A sample prepared by C. L. Liotta was distilled on column number 1.

Methanol-O-d. Material prepared from deuterium oxide and trimethyl borate by R. D. Weimar, Jr. was dried using magnesium metal (19). This material was further dried by a procedure similar to that outlined by Hine and Tanabe (20) for the drying of isopropyl alcohol.

Two liters of methanol-O-d was allowed to react with 20 g. (0.9 mole) of sodium metal and then 119 g. (0.61 mole) of distilled dimethylphthalate was added. The solution was refluxed under nitrogen for 5 days in column number 2 and then distilled.

Preparation of Methyl Acetate. Two hundred milliliters of methanol and 102 g. (1.0 mole) of acetic anhydride was allowed to stand for one day and then distilled. The product was washed with water, dried over Drierite, and distilled on column number 1. Analysis by g.l.c. using a PDEAS column showed no impurity.

Synthesis of Methyl Butyrate. This was prepared from butyric acid and methanol using methyl orthoformate as drying agent[1]. The crude product was further treated with 0.2 mole fraction of water, and a trace of

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[1] This esterification procedure is exemplified for this and following preparations by the synthesis of methyl methoxyacetate given in this section.

19. L. F. Fieser, "Experiments in Organic Chemistry," 3rd ed., D. C. Heath and Co., Boston, 1955, p. 289.

20. J. Hine, and K. Tanabe, J. Phys. Chem., 62, 1463 (1958).

sulfuric acid at 0° for two hours in order to free it of methyl orthoformate. This was washed with saturated sodium bicarbonate, washed with water, dried over Drierite and distilled on column number 1. The material was judged pure by analysis on g.l.c. instrument number 1 using a PDEAS column.

Synthesis of Methyl 3-Ethoxypropionate. Aldrich Chemical Company 3-ethoxypropionic acid was converted to the methyl ester by the use of diazomethane. The resulting solution of the ester in ether was dried over magnesium sulfate and then distilled on column number 1 at 20 mm. pressure. The material was judged pure by analysis on g.l.c. instrument number 2 using a silicone grease column.

Synthesis of Methyl Fluoroacetate. A mixture of 92.4 g. (0.50 mole) of silver fluoroacetate and 62.2 ml. (1.0 mole) of methyl iodide was stirred under reflux for six hours. Ether, 50 ml. was then added, the mixture filtered, and the solution distilled on column number 1. A total of 15 g. of product was collected.

Synthesis of Methyl Hydrocinnamate. This was prepared from hydrocinnamic acid and methanol, using methyl orthoformate as drying agent, in 75 per cent yield. The material was judged pure by analysis on g.l.c. instrument number 1 using a PDEAS column.

Synthesis of Methyl Methoxyacetate. A mixture of 45 g. (0.50 mole) of methoxyacetic acid, 8.0 ml. of dry methanol, 53 g. (0.50 mole) of methyl orthoformate, and five drops of sulfuric acid was refluxed ten hours, then diluted with water and extracted with ether. The ether solution was washed with saturared sodium bicarbonate solution, with

water, and then distilled on column number 1 to give 39 g. of product in 75 per cent yield. A center cut was judged pure by analysis on g.l.c. instrument number 1 using a PDEAS column.

Synthesis of Methyl Propionate. A solution of 160 g. (1.23 mole) of Eastman propionic anhydride and five drops of concentrated sulfuric acid was placed in a flask fitted with a reflux condenser and 32 g. (1.00 mole) of dry methanol was slowly added. The solution was refluxed for one hour and then distilled. A fraction boiling 80 to 95° was collected. The distillate was washed with sodium bicarbonate solution, washed with water, and then distilled on column number 1. A total of 35 g. of methyl propionate was collected in 47 per cent yield.

Preparation of Sodium Methoxide-Methanol-O-d Solutions. Sodium metal was cut under n-pentane and placed under nitrogen in a dry 60 ml. bottle with septum. The bottle was warmed and a stream of nitrogen was used to purge the n-pentane from the bottle. A small amount of methanol-O-d was injected and the flask was vented with a hypodermic needle while maintaining a small positive pressure of nitrogen. After the sodium metal attained a highly lusterous surface, the liquid was removed with a syringe and the required amount of methanol-O-d added with cooling. The bottles were stored over phosporous pentaoxide in a desicator.

Preparation of standard Acids and Bases. The methanolic solutions of p-toluenesulfonic acid and sodium methoxide were prepared by standard techniques. The methanol employed was stock methanol which had been degassed with nitrogen. Titration of stock acids and bases gave only one sharp break in the pH curve. Standardization was against aqueous solutions of standard hydrochloric acid and standard sodium hydroxide.

Table 1. Boiling Points of Some Chemicals Used

Compounds	Observed Value[a]	Literature Value
Methyl Acetate	55-55.5°	56.32° (21)
Methyl Butyrate	101.5-102°	102.65° (22)
Methyl 3-Ethoxypropionate	59-60° (20 mm.)	60° (20 mm.) (23)
Methyl Fluoroacetate	102-103°	103-103.5° (24)
Methyl Hydrocinnamate	150-151° (8 mm.)	236.6° (25)
Methyl Methoxyacetate	128-129°	129.5-130.5° (26)
Methyl Propionate	77.5-78°	79.78-79.98° (27)

[a]Median atmospheric pressure is about 742 mm.

21. M. Wojciechowski and E. R. Smith, J. Research Natl. Bur. Standards, 18, 499 (1937).

22. M. Lecat, Ann. Soc. Sci. Bruxelle. Ser. I, 45, 291 (1926).

23. C. E. Rehberg, M. B. Dixon, and C. H. Fisher, J. Am. Chem. Soc., 68, 544 (1946).

24. C. E. Redemann, S. W. Chaikin, R. B. Fearing, G. J. Rotariu, J. Savit, D. Van Hoesen, ibid., 70, 3604 (1948).

25. F. Weger, Ann. Chem., 221, 61 (1883).

26. J. Pryde and R. T. Williams, J. Chem. Soc., 1627 (1933).

27. J. H. Mathews, J. Am. Chem. Soc., 48, 562 (1926).

Instrumentation

Distillation Columns

Two distillation columns were used. Column number 1 was a Nester-Faust Intermediate Spinning Band Column. The efficiency of this column is said by the manufacturer to be 30 theroretical plates. Column number 2 was a Todd Precision Fractionation Column with a 2 cm. diameter body packed with glass helices. The efficiency is said to be 20 theoretical plates by the manufacturer.

Gas-Liquid Chromatography Instruments

Three gas-liquid chromatography instruments were used. Instrument number 1 was a Wilkens Model A-70 Preparative Gas Chromatograph. Helium was used as the carrier gas. The recommended operating procedures were followed. Carrier gas flow rates of 70 ml. per minute and 120 ml. per minute were used with the 1/4 and 3/8 inch diameter columns respectively. Instrument number 2 was a Perkin-Elmer Vapor Fractometer, model 154-D. The instrument was a standard unit using packed columns. Helium was used as the carrier gas. The recommended operating procedures were followed. Instrument number three was a Perkin-Elmer Vapor Fractometer, model 154-D, equipped with a 300 ft. Golay column and a Perkin-Elmer flame ionization detector. The column was packed with Apiezon L and carried the Perkin-Elmer designation of Q. Nitrogen was used as the carrier gas. The recommended operating procedures were used.

Gas-Liquid Chromatography Columns

All columns used with the Perkin-Elmer g.l.c. instrument number 2

were standard Perkin-Elmer products. The packed columns used were made of one-fourth inch stainless steel tubing two meters in length. The word "packed" will be omitted in further references to the packed columns. The columns used were Column A, having a liquid phase of Diisodecylphthalate, Column O, having a liquid phase of silicone grease (Dow Corning 11), and Column Q having a liquid phase of Apiezon L.

Columns used with the Wilkins g.l.c. instrument number 1 were made of three-eighth inch aluminum tubing generally ten feet in length. All columns were packed with 42 to 60 mesh Chromasorb P which had a 30 per cent loading of the liquid phase. The liquid phases used were PDEAS (phenyl diethanolamine succinate). SE-30 (Silicone Gum Rubber, Methyl), Silicone Grease (Dow Corning 11), Carbowax 20M, and diisodecylphthalate. The Carbowax 20M and SE-30 columns were twenty feet in length, the former was one-fourth inch in diameter.

Titration Assembly and pH Meter

A Beckman Zeromatic II pH meter was used with a standard glass electrode and a calomel reference electrode. A beaker containing a magnetic stirring bar was covered with a cork through which the electrodes and burrette were admitted. During titrations a nitrogen stream was directed into the beaker to prevent entrance of atmospheric carbon dioxide.

Infrared Instrument

A Perkin-Elmer Recording Spectrophotometer, Model 21, was used for all quantitative measurements. These measurements were made using an automatic slit control setting of 990, an auto suppression of five, a

response of two, a chart speed of 0.6 microns per minute, and 0.005 cm. sodium chloride cells.

Constant-Temperature Bath

A Sargent constant-temperature water bath was used. The temperature was adjusted to 35.0 ± 0.2° by means of a -10 to 100° thermometer with 0.5° divisions and certified by the National Bureau of Standards. Fluctuations about this temperature were not noticeable on a thermometer with graduations of 0.1°.

Boiling Point Determinations

Boiling points recorded were taken as the distillation temperature of the fraction collected. All boiling points reported herein are uncorrected.

Nuclear Magnetic Resonance Spectrometer

A Varian Nuclear Magnetic Resonance Spectrometer, model A-60, was used. Chemical shifts were determined using tetramethylsilane as an internal standard. The machine was operated in accordance with the instruction manual.

Quantitative Infrared Spectrometry

The method used to determine the molar concentration of methanol in methanol-O-d was according to the procedure of Duke (28). Methanol in

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28. R. B. Duke, Thesis, Georgia Institute of Technology, to be published.

methanol-O-d has a strong polymeric associated OH stretching band at 3360 cm^{-1} which can be used to determine the concentration of methanol directly. The absorbance of this band is determined in the following manner. The spectrometer is set to 3900 cm^{-1} and scanned to 3000 cm^{-1}. Prior to the absorption band a minimum absorption region is encountered which is very nearly a transparent region. The absorbance of the band is taken as the differnece between this minimum and the maximum absorbance values. The band is rather broad so that maximum absorbance is well defined and quite reproducible. Scans on the same sample reproduce an absorbance value of 0.500 units with a variation of not more than $\pm$ 0.002 units.

The sodium chloride windows are dissolved slowly by methanol solutions so it is necessary to make periodic measurements of the cell thickness. The 1960 cm^{-1} band of benzene is used for this purpose as suggested by the instrument manufacturer. This region of the spectrum is scanned with benzene in the cell and a straight line is drawn tangent to the spectral curve on both sides of the absorption maximum. The absorbance value is defined as the difference between the maximum value and that of the base line defined by the straight line. The cell thickness is then given by the equation $l_{(cm^{-1})} = 0.0100$ A.

Due to the sharpness of this band and the rather wide slit width employed, it was found that the cell thicknesses, so determined, do not vary linearly with true cell thickness. This was determined by testing Beer's law for benzene in carbon tetrachloride and by testing Lambert's law for a 20 per cent solution of benzene in carbon tetrachloride. The latter experiment was carried out with a Perkin-Elmer variable thichness

cell with a micrometer adjustment. The data for these experiments are presented in tables 2 and 3 and the data are plotted in Figure 1. Both curves are superimposable and indicate a decreasing rate of absorbance as the cell thickness is increased. This factor introduces an error of about ± 2.5 per cent into cell thickness determinations when the thicknesses are kept within the range of 0.0049 to 0.0068 cm.

The values (28) for the extinction coefficient of the 3360 cm^{-1} band of methanol as a function of sodium methoxide concentration are given by the equation

$$\epsilon = 137.3 - 13.1[CH_3ONa] \qquad (1)$$

where $$0 < [CH_3ONa] < 0.65,$$

and are based on cell thickness determined using benzene as has been described. Using these values, the molar concentration of protiomethanol in sodium methoxide-methanol-O-d solutions is given by

$$[CH_3OH] = A_{obs} / l_{(cm)} \epsilon \ . \qquad (2)$$

Samples of the solution to be analyzed were carried to the spectrometer in a hypodermic syringe with needle attached, the needle was removed, the ground glass tip of the syringe wiped free of liquid, and quickly inserted into the cell receptacle. After filling and closing the cell, the syringe was inserted back into the needle and emptied of all its contents. The same syringe could be used for a series of analyses in a

Table 2. Beer's Law for the 1960 cm^{-1} Band of Benzene in Carbon Tetrachloride

Volume per cent Benzene	Absorbance
0	0.000 ± 0.000
20	0.182 ± 0.000
40	0.330 ± 0.001
60	0.452 ± 0.001
80	0.560 ± 0.002
100	0.671 ± 0.002

Table 3. Lambert's Law for the 1960 cm^{-1} Band of Benzene, 20 Volume Per Cent in Carbon Tetrachloride

l (mm)	Absorbance
0.030	0.048
0.090	0.130
0.140	0.207
0.190	0.278
0.240	0.341
0.290	0.405
0.340	0.453
0.415	0.535
0.540	0.652
0.790	0.836
1.040	1.05

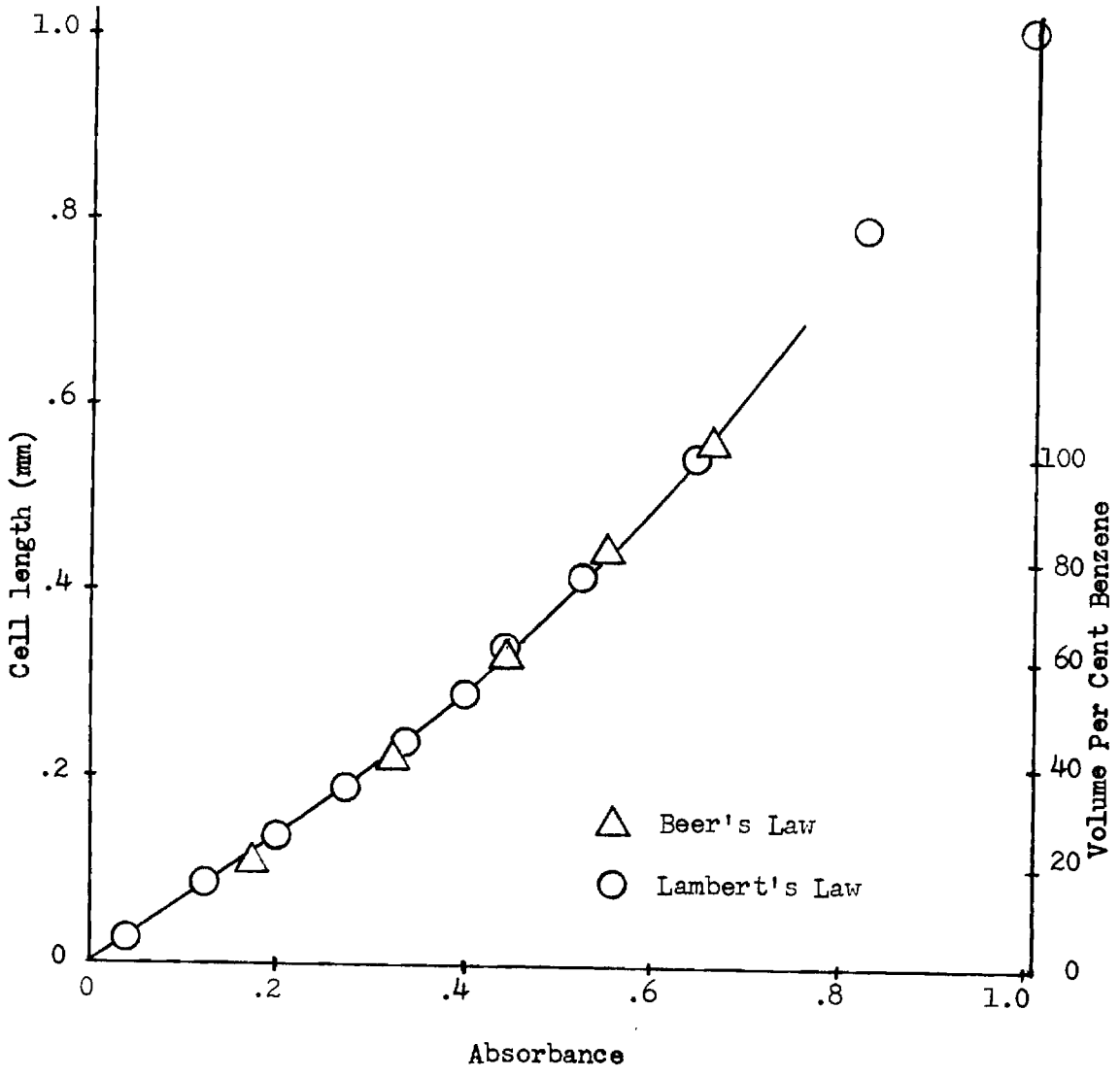

Figure 1. Beer's and Lambert's Laws for the 1960 cm^{-1} Band of Benzene in Carbon Tetrachloride.

given kinetic run provided no air was drawn into the barrel from the atmosphere and provided it was flushed twice with approximately 0.20 ml. of kinetic solution prior to sampling.

The cell was flushed with approximately five milliliters of carbon tetrachloride after analysis and then dried with a stream of dry nitrogen. The cell was then placed in a desiccator until the next analysis. Cells were rebuilt using 0.005 cm. spacers when the cell thickness exceeded about 0.0068 cm.

Titration of Base Solutions

During the course of kinetic runs the base concentration must be determined in order to account for side reactions. The procedure adopted was to quench one to two milliliters of the kinetic solution with a slight excess of standard p-toluenesulfonic acid in methanol, and then to titrate the excess acid with standard sodium methoxide solution using a pH meter. The use of p-toluenesulfonic acid gave reasonable acid stability when stored between use in the freezer chest of the refrigerator.

The concentration of sodium methoxide and of most of the conjugate bases of the weaker acids could be obtained from a plot of pH versus volume of standard base. Small amounts of weak bases could be detected in some runs; these were probably formed from small amounts of water, which result in ester hydrolysis. Even in runs in which the sodium methoxide concentration was relatively small, the base consumption was not troublesome; the change in sodium methoxide concentration was always less than three per cent during the time that kinetic measurements were made. Sufficiently precise rate constants could be gotten by using the average

base concentration for any one run.

Treatment of Kinetic Data

Base catalyzed deuterium exchange of the alpha protons of esters follows simple pseudo first-order kinetics since the base is not consumed during the reaction to any appreciable extent. The reaction proceeds with an increase in the concentration of protiomethanol, which is observed directly as an increase in the absorbance of the 3360 cm^{-1} band in the infrared region. This observed absorbance value is corrected to a cell thickness of 0.0100 cm. and is used as a direct measure of the extent of reaction. The corrected absorbance, A, is governed at zero time by the isotopic purity of the methanol-O-d solution and at infinite time by the equilibrium concentration of exchangeable protio-hydrogen.

Using the equation for first order kinetics,

$$\log \frac{A_\infty - A_o}{A_\infty - A} = 2.303\ k_a\ t\ , \qquad (3)$$

a plot of the log factor versus time should give a straight line passing through the origin and having a slope of $2.303/k_a$. Thus the apparent first-order rate constant was obtained from the slope of the best line through the kinetic points by substitution into

$$k_a = 2.303/\text{slope}. \qquad (4)$$

The apparent second-order rate constant, k, for sodium methoxide catalyzed

exchange is then found by substitution of k_a and the base concentration into

$$k = k_a/[NaOCH_3]. \tag{5}$$

The relation between k and the true rate constant for the attack of methoxide ion upon alpha protons is discussed in the results and discussion section. The value of A_∞ was in all cases a calculated value assuming random distribution of all exchangeable deuterium and protium atoms. Hence at equilibrium the total concentration of protiomethanol is

$$[CH_3OH]_\infty = [CH_3OH]_o + n[\text{Ester}](\text{fraction of alpha-hydrogen exchanged})$$

or

$$[CH_3OH]_\infty = [CH_3OH]_o + n[\text{Ester}]\frac{[D]}{[H] + [D]} \tag{6}$$

where [H] and [D] are the total molar concentration of exchangeable protium and deuterium respectively and where n is the number of alpha protons in the ester. The value of [D] can be approximated as the molar concentration of methanol, protio and deutero, or very nearly 24 for dilute solutions. The equation then becomes

$$[CH_3OH]_\infty = [CH_3OH]_o + n[\text{Ester}]\frac{24}{n[\text{Ester}] + [CH_3OH]_o + 24}. \tag{7}$$

The factor in the last part of this equation is the calculated fraction of total deuterium exchange occuring in the ester at infinite time and for most runs has the value of approximately 0.95.

The observed absorbance for most runs began at about 0.25 units and were followed up to about 0.9 units. The accuracy of the optical wedge is said to be linear to 1/2 per cent transmittance units over this region so that at 0.6 absorbance units the error is $\pm$ 0.009 units, at 0.8 units the error is $\pm$ 0.014 units, and at 0.9 units the error is $\pm$ 0.018 units. This would give a probable error of about $\pm$ 5 per cent in the determination of rate constants, but as will be seen, the data appear to be better than this.

General Kinetic Procedure

The procedure for dimethyl succinate will be given here as an illustration of the general kinetic procedure. The molar concentrations determined are all at 25°, since the extinction coefficients were determined at room termperature. The error introduced by this procedure is well within the overall experimental error.

The kinetic flask was an oven dried, 25 ml. erlenmeyer flask fitted with a rubber septum. The flask has been purged with nitrogen and the rubber septum had been digested with acetone, dried with a hot air gun, and stored in a desiccator over silica gel. All syringes were dried in the same manner.

Using syringes, 1.1760 g. of 0.34 molar sodium methoxide-methanol-O-d solution and 8.248 g. of methanol-O-d were added to the flask. It was necessary to vent the flask during these additions to allow accurate

dispensing of the ester which followed. The weight error due to venting is not significant compared to the weights of methanol-O-d solutions used. A 0.5 ml. syringe was used to inject 0.33 ml. (0.3667 g.) of dimethyl succinate into the flask and, after weighing, the flask was placed in the 35.0° bath and agitated for one minute. The timer was started when the flask entered the bath. The time interval between injection of ester and placement in the bath was less than one minute. Samples of the solution were taken at intervals and carried to the infrared instrument for analyses, the time interval between sampling and analysis being about two minutes.

The data were reduced in the following manner. Using densities of sodium methoxide-methanol-O-d solutions which were estimated from the data in Table 29, the total volume is 11.92 ml. at 25°. The molar concentration of dimethyl succinate is then 0.2102. The corrected absorbance, A, of methanol at time zero is estimated by extrapolation to be 0.500 and using the extinction coefficient of methanol for the determined sodium methoxide concentration of 0.0431, the initial methanol concentration is calculated by means of equation 2 to be 0.365. Equations 2 and 7 give the value of methanol concentration and the value of the absorbance, both at infinite time, to be 1.165 and 1.596 respectively. The kinetic data are presented in Table 14 and are plotted in Figure 2.

Investigation of Alkoxy Exchange for Methyl 3-Ethoxypropionate

There is a possibility that methyl 3-methoxypropionate undergoes methoxide ion catalyzed deuterium exchange by an elimination-addition mechanism. This possibility was investigated by treating methyl

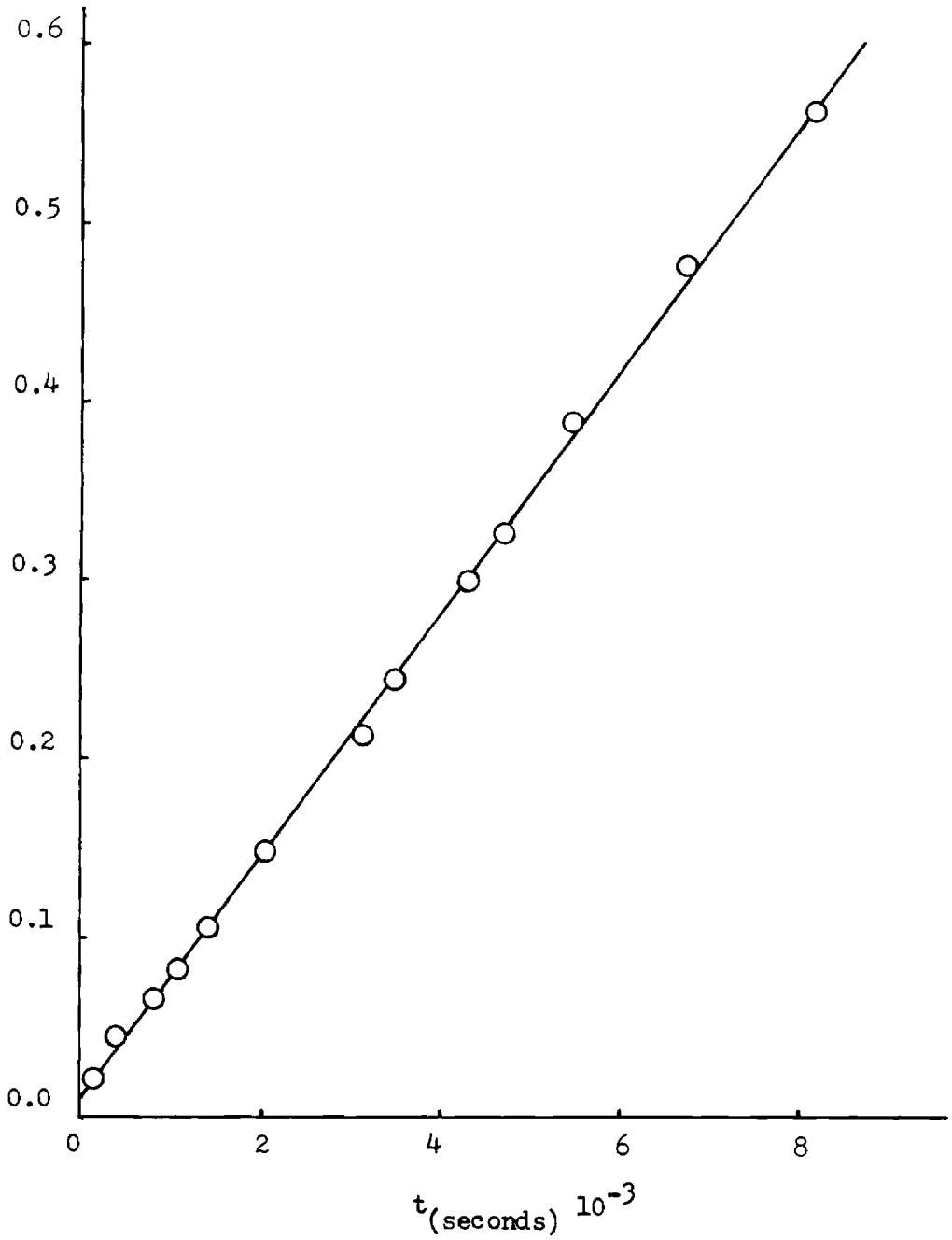

Figure 2. Kinetics of the Deuterium Exchange of Dimethyl Succinate at 35° with a Sodium Methoxide Concentration of 0.0431 M

3-ethoxypropionate with sodium methoxide in methanol-O-d and examining the product for methyl 3-methoxypropionate.

A methanol-O-d solution (3.00 ml.) was prepared containing 0.45 M methyl 3-ethoxypropionate and 0.14 M sodium methoxide. The solution was placed in a 35.0° bath for 560 seconds (this would result in 40 per cent deuterium exchange if the second-order rate constant was 3.0×10^{-3} M^{-1} sec^{-1}) and then was quenched with the calculated amount (0.50 ml.) of 0.92 M hydrochloric acid. The resulting solution was concentrated to ca. 2 ml. under a nitrogen stream and combined with 5 ml. of pH 7 buffer solution. The mixture was extracted with three 1.0 ml. portions of chloroform. The chloroform extract was concentrated under a nitrogen stream and then examined on g.l.c. instrument number 2 using a silicone grease column at 135°. A peak appeared at 6.5 min. which was due to methyl 3-ethoxypropionate but no peak was found for methyl 3-methoxypropionate, which has a retention time of 4.6 min. An estimate of the minimum ratio of the ethoxy ester to the methoxy ester is about 1000:2.

The rate of deuterium exchange of methyl 3-ethoxypropionate was roughly measured by preparing a solution from 0.0941 g. of methyl 3-ethoxypropionate and 2.00 ml. of 0.42 M sodium methoxide in methanol-O-d. This was quickly placed in an infrared cell and absorbance was measured at a fixed wavelength of 1960 cm^{-1}. The half-life was approximately 350 sec. (Table 27) which gives a second-order rate of ca. 5×10^{-3} M^{-1} sec^{-1}. The temperature of the cell was estimated to be about 30-35°.

These data show that the removal of an alpha proton from methyl 3-ethoxypropionate by methoxide ion results in exchange of the ethoxy

groups less than 1/200th. of the time.

Kinetics of the Drying of Methanol

Drying of methanol, using sodium methoxide and dimethyl phthalate, requires a knowledge of the rate of the reaction in order that conditions can be chosen which will assure complete drying. The required rate constant was determined in the following manner.

In an oven dried 100 ml. volumetric flask was placed a solution of 0.30 g. of sodium metal in 50 ml. of dry methanol[1], 3.88 g. (0.0200 mole) of distilled dimethyl phthalate, 0.340 g. (0.0189 mole) of water, and sufficient dry methanol to make up the mark. The solution was pipetted by automatic syringe, 3.92 ml., into ampoules which were then sealed under nitrogen. The ampoules were suspended above refluxing methanol (64.5°) at T_o and removed at time intervals. The ampoules were broken and the solution washed into 5.00 ml. portions of 0.1022 N hydrochloric acid. The excess acid was then determined by titration with 0.0986 N sodium hydroxide solution using phenolphthalein as indicator.

The overall reaction is :

$$CH_3ONa + H_2O \underset{}{\overset{K}{\rightleftharpoons}} NaOH + CH_3OH$$

$$NaOH + RCO_2CH_3 \overset{k}{\rightleftharpoons} CH_3OH + RCO_2Na$$

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[1] The procedure is the same as that described for methanol-O-d.

The value of K at 25° is 0.22 and should not be much different at 64.5° (29). The total base concentration, B, can be taken, to a good approximation, as the sodium methoxide concentration.

$$[NaOH] = \frac{K[CH_3ONa][H_2O]}{[CH_3OH]^2} \approx \frac{KB[H_2O]}{24^2} \qquad (8)$$

The rate for the bimolecular attack of hydroxide on the ester can be expressed in terms of a third order reaction.

$$-\frac{d[Ester]}{dt} = -\frac{d[H_2O]}{dt} = kKB[H_2O][Ester]/24 \qquad (9)$$

The attack of hydroxide upon the second ester group is not considered as this would be expected to be much slower than on the first ester group. Integration yields:

$$\frac{1}{(E - B)(W - B)} \log \left(\frac{B}{B - x}\right) + \frac{1}{(B - W)(E - W)} \log \left(\frac{W}{W - x}\right) + \frac{1}{(B - E)(W - E)} \log \left(\frac{E}{E - x}\right) = \frac{kKt}{2.3 \cdot 24} \qquad (10)$$

where B, E, and W refer to the initial concentrations of total base, ester, and water respectively.

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29. J. Murto, Suomen Kemistilehti, 35B, 157 (1962).

This data are presented in Table 28 and the product kK was found to be 6.0×10^{-2} $l^2 m^{-2} s^{-1}$. For the purpose of drying methanol, where the initial water concentration is very small, the kinetics can be described as a pseudo first order reaction. The water concentration is

$$\log \frac{W}{W_o} = \frac{(6.0 \times 10^{-2})BE}{24} t \qquad (11)$$

one thousandth of its initial concentration after 3.1 hours at reflux using a base concentration and an ester concentration of 0.5 molar. This assumes no reversibility of the drying process.

CHAPTER III

RESULTS AND DISCUSSION

Kinetic Results

The results of the sodium methoxide catalyzed deuterium exchange studies are presented in Table 4. The reproducibility of the data, for most compounds, is seen to be within about six per cent. Many of the duplicate rate constants were determined using an approximately two-fold variation in sodium methoxide concentration. The consistency of the second-order rate constants observed for these duplicate determinations verify the simple first order catalysis by sodium methoxide. This appears to be true for sodium methoxide concentrations up to at least 0.579 M, as shown by data for methyl butyrate, and probably is true for the entire concentration range employed since the maximum concentration used was only 0.644 M.

An effort was made to preserve the methanolic character of the solvent throughout all kinetic runs by holding the volume per cent of ester to about three per cent; however, esters having higher molecular weights and only one exchangeable proton made this difficult to achieve. Methyl dimethoxyacetate and methyl difluoroacetate require kinetic solutions of about ten volume per cent of ester for accurate kinetic measurements. A smaller volume per cent of methyl difluoroacetate leads to a less precise value of the rate constant as is shown by the data of

Table 24.

The difficulty of accurately determining sodium methoxide concentrations of less than about 0.010 M sets an upper limit for second-order rate constants of about 10^{-2} M^{-1} sec^{-1}. In this regard the data for methyl phenylacetate, Table 26, is highly questionable. The sodium methoxide concentration indicated in this case is the calculated initial value and was not determined during the course of the deuterium exchange reaction. The linearity of the kinetic plot does indicate, however, that the base concentration remained constant during that portion of the reaction observed.

The reactions were routinely followed to about 70 per cent completion and, in the case of methyl 3-methoxypropionate, Table 13, to greater than 90 per cent completion without observing a tendency towards falling first-order rates. This is significant as it demonstrates the absence of a complicating influence of primary and secondary kinetic isotope effects.

A complete description of the kinetic form for these reactions, which would include isotope effects, is best accomplished by two separate discussions. The first will take into account the reversibility of the reaction as well as the influence of primary kinetic isotope effects upon the fate of the intermediate carbanion. The second will treat those systems which have more than one hydrogen atom per molecule available for exchange and will consider the influence of secondary kinetic isotope effects.

The exchange reaction for molecules bearing one exchangeable proton

can be expressed in terms of the following steps:

$$HA + CH_3O^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} A^- + CH_3OH$$

$$A^- + CH_3OD \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} DA + CH_3O^-$$

Since the carbanion, A^-, is present in only relatively small concentrations it is apparent that $k_{-1} >> k_1$ and $k_2 >> k_{-2}$. The fraction k_{-1}/k_2 is the primary kinetic isotope effect for the transfer of a hydrogen ion from methanol to the carbanion. It is assumed that diffusion of methanol and methanol-O-d to and from the carbanion is sufficiently fast that it may be neglected in the kinetic treatment. The net rate of the forward reaction can then be written:

$$-\frac{d[HA]}{dt} = [CH_3O^-]\frac{k_1k_2[CH_3OD][HA] - k_{-1}k_{-2}[CH_3OH][DA]}{k_2[CH_3OD] + k_{-1}[CH_3OH]} \qquad (1)$$

The equilibrium constant for the overall reaction is $k_1k_2/k_{-1}k_{-2}$ and should be very nearly unity for such an isotopic redistribution process (30). Using this and the relations $i = k_{-1}/k_2$, $x = -d[HA]$, $a = [HA]_o$, $[DA]_o = 0$, $P = [CH_3OH]_o$, and $s = [CH_3OD]_o$, the unintegrated rate equation becomes:

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30. H. Bolder, G. Dallinga, and H. Kloosterziel, J. Catalysis, 3, 312 (1964).

$$\frac{dx}{dt} = k_1[CH_3O^-]\frac{(a - x)(s - x) - x(p + x)}{i(p + x) + (s - x)} \qquad (2)$$

Integration of this equation gives:

$$2.303\left[\frac{s + ip}{a + s + p} + \frac{as(i - 1)}{(a + s + p)^2}\right]\log\left[\frac{a}{a - \frac{(a + s + p)x}{s}}\right]$$

$$- \frac{(i - 1)x}{a + s + p} = k_1[CH_3O^-]\ t \qquad (3)$$

An approximating equation can be obtained from the exact equation by setting $\underline{i}$ equal to one.

$$2.303\left(\frac{s + p}{a + s + p}\right)\log\left[\frac{a}{a - \frac{(a + s + p)x}{s}}\right] = k_1[CH_3O^-]\ t \qquad (4)$$

The equation used to evaluate rate constants omitted the factor (s+p)/(a+s+p) from Equation 4 and is written

$$2.303\log\left[\frac{a}{a - \frac{(a + s + p)x}{s}}\right] = k[CH_3O^-]\ t \qquad (5)$$

which is equivalent to

$$2.303\log\left[\frac{A_\infty - A_o}{A_\infty - A}\right] = k[CH_3O^-]\ t \qquad (6)$$

where k is the apparent second-order rate constant and A is absorbance.

The coefficient of the log term in Equation 4 decreases as a is increased, but it would not vary more than about eight per cent among the kinetic runs. An examination of duplicate rate determinations shows, however, that the apparent second-order rate constants decrease, in general, as a is made larger. This behavior is opposite to that predicted by Equation 4 and is probably due to neglect of primary isotope effects. This can be seen by reference to Equation 3. The log coefficient of Equation 3 is

$$2.303 \frac{s + ip}{a + s + p} + \frac{as(i - 1)}{(a + s + p)^2}$$

and includes kinetic isotope effects. The value of this coefficient is insensitive to the value of a when i is about two and increases as a is increased when i is about six.

The validity of the equation used to determine rate constants was tested by generating hypothetical data by means of Equation 3 and plotting this data using Equation 5. The results are given in Figure 3 where a kinetic isotope effect of ten was imposed. The graphically determined slopes do not differ more than two per cent between the cases where a is 1 M and where a is 2 M. Although the downward curvature of the plot is greater when a is large, this if offset by using an earlier portion of the plot for the graphical solution.

In the event that the primary kinetic isotope is less than ten and is constant for all compounds studied, Equation 5 or 6 will give

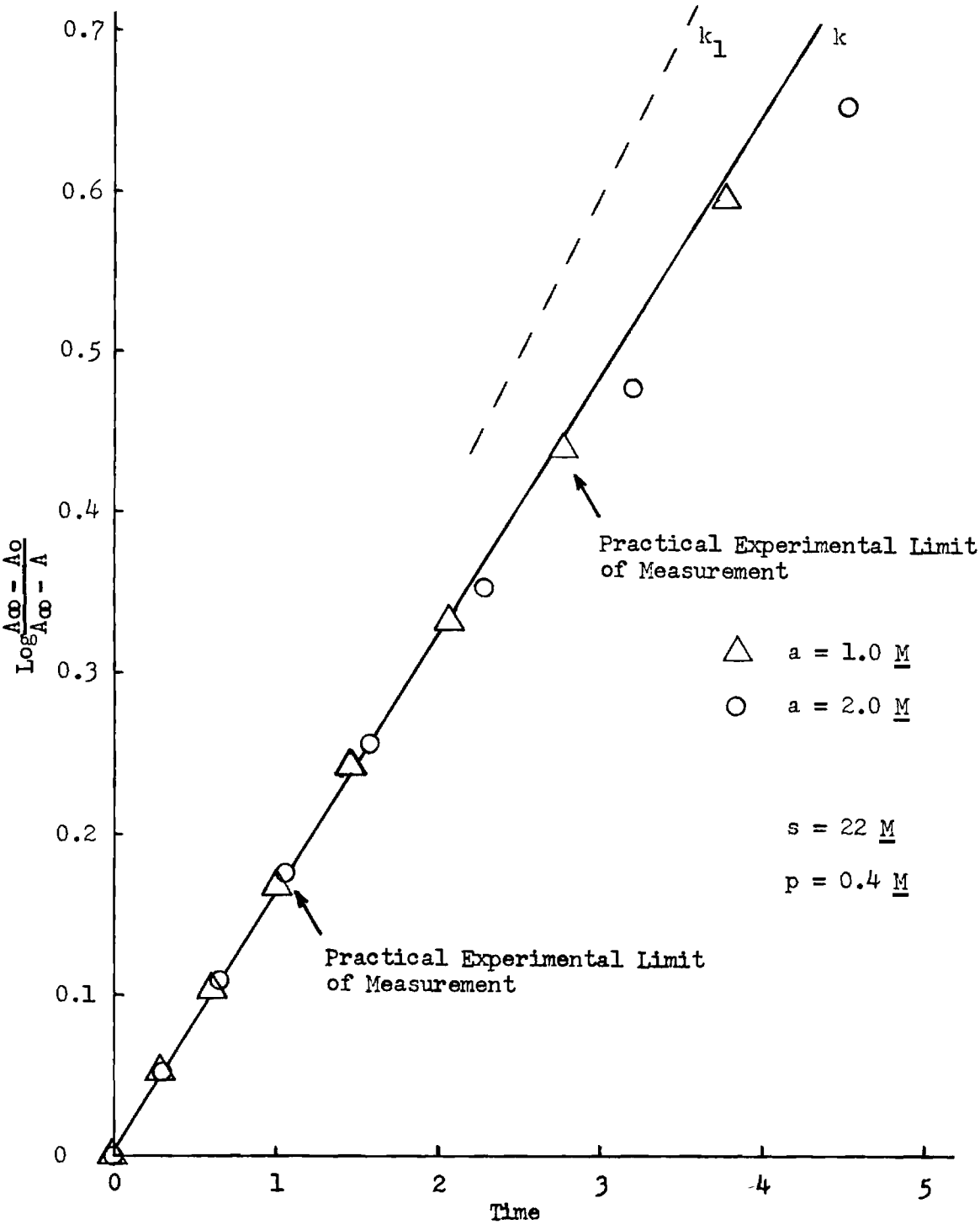

Figure 3. Plot of Hypothetical Deuterium Exchange Data Imposing a Kinetic Isotope Effect of Ten

relative rate constants, which are within the experimental errors arising from other causes. The apparent second-order rate constants thus obtained can be related to $\underline{k}_1$, the true second-order rate constant, only if the value of $\underline{i}$ is known. As an example, Figure 3 shows that $\underline{k}$ is about 0.8 $\underline{k}_1$ when $\underline{i}$ is ten. Of course $\underline{k}$ would equal $\underline{k}_1$ when $\underline{i}$ is one.

Compounds which contain multiple alpha-protons can be considered in terms of a stepwise process.

$$AH_3 \xrightarrow{k'_1} AH_2D$$

$$AH_2D \xrightarrow{k'_2} AHD_2$$

$$AHD_2 \xrightarrow{k'_3} AD_3$$

where $\underline{k}'_1$ and $\underline{k}'_2$ are rate constants for the bimolecular attack of methoxide ion upon hydrogen. In as far as the reactivity of a proton is independent of the identity of its neighboring hydrogen, proton or deuteron, (i.e. absence of a secondary kinetic isotope effect) the rate constant for the overall exchange process represents a statistically corrected rate constant (31) equal to $\underline{k}'_1/3$, $\underline{k}'_2/2$, or $\underline{k}'_3$. The reported values of secondary kinetic isotope effects for substitution of a deuterium atom on a carbon which is undergoing a change from $\underline{sp}^3$ to $\underline{sp}^2$ hybridization is about 1.1 per deuterium atom (32). These results

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31. S. W. Benson, J. Am. Chem. Soc., 80, 5151 (1958).

32. W. A. Pryor, R. W. Henderson, R. A. Patsiga, and N. Carroll, J. Am. Chem. Soc., 88, 1199 (1966) and references therein.

have been rationalized as arising primarily from zero-point virbrational energy changes during the course of the reaction (33).

In the study at hand, the complicating influence of secondary kinetic isotope effects do not appear to be troublesome, since no kinetic plot shows a rate decrease greater than eight per cent at half reaction. Graphical determination of rate constants probably reduces this type of error to within the experimental error due to other causes.

Taft Correlation of Rate Constants

A correlation of the second-order rate constants of Table 5 by means of the Taft equation is not totally adequate. In Figure 4 the logs of the rate constants are plotted against the sum of the Taft polar substituent constants σ^*_X and σ^*_Y for the ester $XYCHCO_2CH_3$. For most of the substituents σ^* values are directly available, but for three of the substituents the useful but fallible generalization that $\sigma^*_X = 2.8\ \sigma^*_{XCH_2}$ was employed (34). Thus $\sigma^*_{CH_3O}$ and σ^*_F were taken as 2.8 times $\sigma^*_{CH_3OCH_2}$ and $\sigma^*_{FCH_2}$ respectively, and $\sigma^*_{CH_3O_2CCH_2}$ was taken as 1/2.8 times $\sigma^*_{CH_3O_2C}$. A reasonable Taft correlation exists only for the cases in which X is H and Y is Et, Me, $PhCH_2$, H, and MeO_2CCH_2. In figure 5 the log k's for these esters are seen to fall about a

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33. E. A. Holevi, Progr. Phys. Org. Chem., 1, 109 (1963).

34. J. Hine, "Physical Organic Chemistry," 2nd ed., McGraw-Hill Book Co., Inc., New York, 1962, sec 4-4.

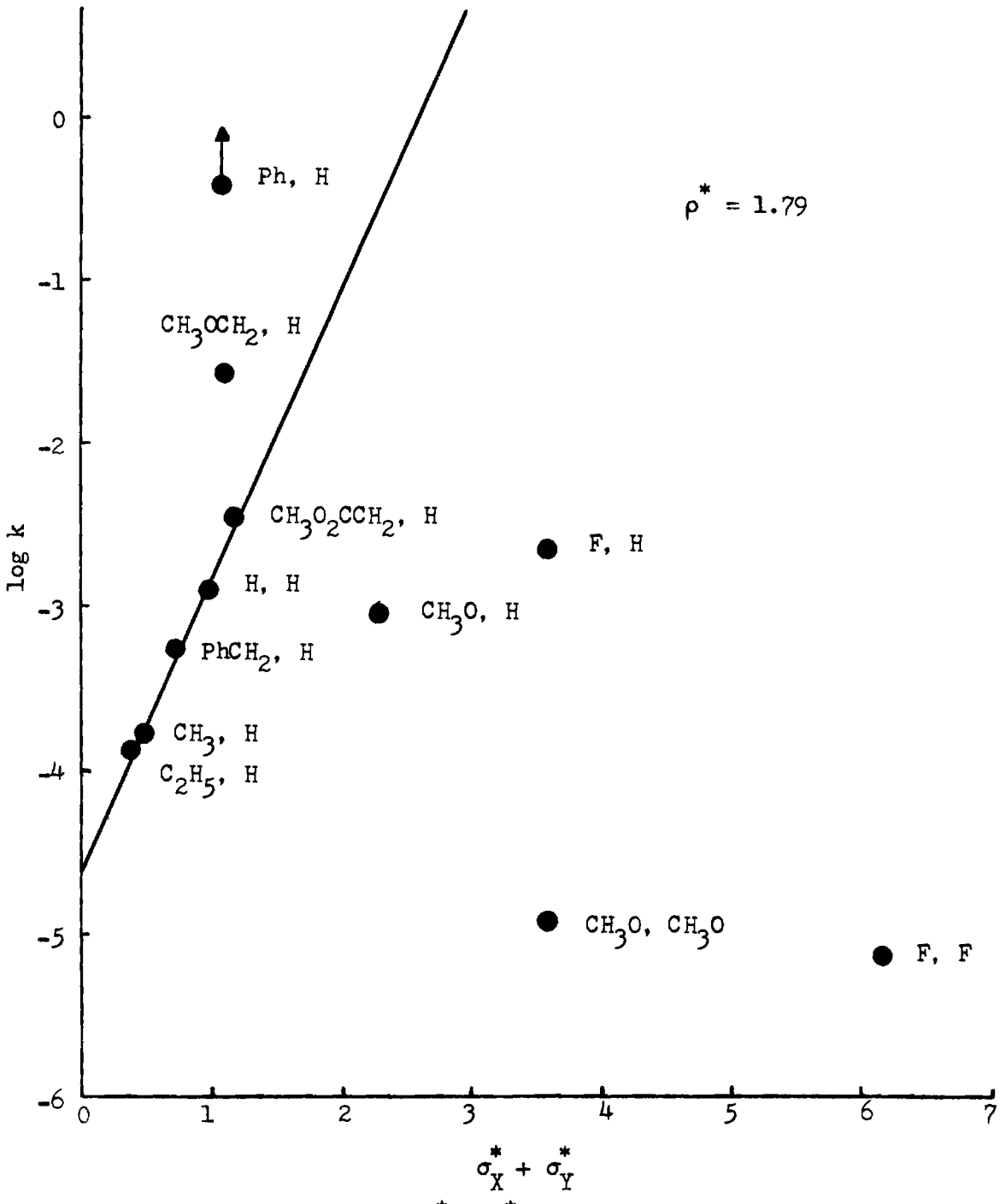

Figure 4. Taft Plot of $\sigma_X^* + \sigma_Y^*$ vs. Log k for the Esters $XYCHCO_2CH_3$

line defined by Equation 7 with an average deviation of 0.042 log

$$\log k^* = 1.79(\sigma_X^* + \sigma_Y^*) - 4.604 \qquad (7$$

units. The compounds used to define this equation have substituent groups which are probably free of complicating steric and resonance effects which might lead to deviations from the Taft equation; therefore, in further discussions, this equation will be used to evaluate the polar effect of alpha substituents upon the reaction rate.

The best line through the eleven points in Figure 4 would have a negative slope; however, such a line, corresponding to destabilization of the transition state by electron withdrawing substituents, does not give a pausible picture of the polar effect of substituents upon carbanion formation. The rate controlling step in all of the reactions has the form:

$$XYCHCO_2CH_3 + CH_3O^- \longrightarrow \overset{-}{X}YCCO_2CH_3 + CH_3OH$$

The value ρ^* for this reaction would be expected to be positive and less than the ρ^* value of about 3.2 which was observed for the acidity of ammonium ions (35). The smaller ρ^* value of 1.79 for the present case is due in part to development of less than a full negative charge in the transition state in part to delocalization of the negative charge onto

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35. H. K. Hall, Jr., J. Am. Chem. Soc., 79, 5441 (1957).

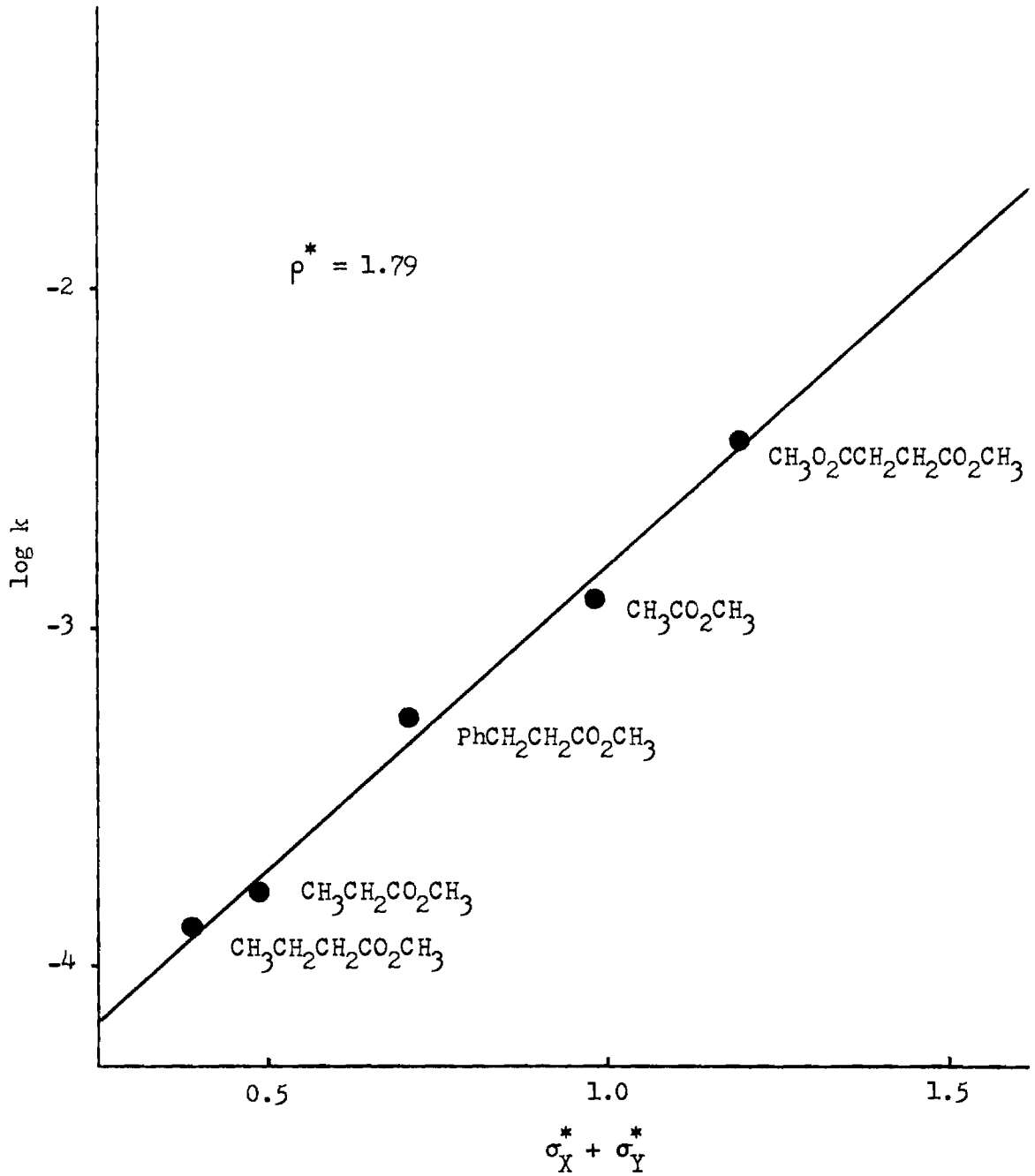

Figure 5. Taft Plot of Monosubstituted Acetates of the Type $XYCHCO_2CH_3$

the more electronegative oxygen atom, whereas in the ionization of ammonium ions a full positive charge is localized largely on nitrogen. The ρ^* value for base-catalyzed bromination of ketones of the type $R_1R_2CHCOPh$ is 1.59 in water at 25° (36). This reaction involves formation of the enolate anion in the rate controlling step and is quite similar to the reaction at hand.

The positive deviation (2.3 log units) of methyl phenylacetate from the Taft correlation can be rationalized in terms of resonance delocalization of the negative charge of the intermediate enolate anion by the phenyl group. This is a cross-conjugated system in which the conjugation with the carbonyl group presumably would be larger; therefore, it was not certain, a priori, that resonance stabilization by the phenyl group would be large.

Interestingly, methyl 3-methoxypropionate is also found to deviate (1.0 log units) in a positive direction from the Taft correlation. One possibility for this behavior is that methoxide ion might be eliminated during the formation of the alpha carbanion to give methyl acrylate which would then undergo methoxide catalyzed addition of methanol-O-d. To the extent that removal of the alpha proton proceeds by an E2 elimination-addition mechanism an apparent rate enchancement will result. The observed rate for proton removal will be greater than the "normal" carbanion formation rate by the factor: (fraction of proton removal proceeding by an E2 mechanism)/(fraction of proton removal by the normal mechanism). If less than two per cent of the

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36. D. P. Evans and J. J. Gordon, J. Chem. Soc., 1434 (1938).

total deuterium exchange reaction proceeds by an E2 mechanism, no observable complication by this factor would result. If methanol is eliminated from methyl 3-methoxypropionate it seems reasonable that ethanol should be eliminated from methyl-3-ethoxypropionate also. The latter elimination is more easily detectable since elimination of ethanol in methanol-O-d should result in transformation of methyl 3-ethoxypropionate to methyl 3-methoxypropionate. However, methyl 3-

$$C_2H_5OCH_2CH_2CO_2CH_3 \xrightarrow{CH_3O^-} C_2H_5OH + CH_2{=}CHCO_2CH_3$$

$$CH_3OD + CH_2{=}CHCO_2CH_3 \xrightarrow{CH_3O^-} CH_3OCH_2CHDCO_2CH_3$$

ethoxypropionate was found to undergo base-catalyzed deuterium exchange at a rate at least 200 times greater than the rate for formation of methyl 3-methoxypropionate.

Since deuterium exchange of methyl 3-methoxypropionate is not accompanied by elimination of alcohol, as judged by the ethoxypropionate, the anomolously large reactivity may be due to double bond - no bond resonance (8) stabilization of the carbanion by a structure in which a methoxy group is nonbonded. This negative hyperconjugation effect has been used to explain the ability of beta fluorine atoms to

$$CH_3O\text{-}CH_2\text{-}\dot{C}H\text{-}C(=O)OCH_3 \longleftrightarrow CH_3O^- \; CH_2{=}CH\text{-}C(=O)OCH_3$$

stabilize carbanions (37). Note also that the 160-fold factor by which a beta methoxy group increases the rate of carbanion formation over a beta hydrogen is smaller than the 500-fold effect observed in the case of a beta methoxy group trans to the hydrogen being removed in cyclohexyl p-tolylsulfone (38). Although the trans stereochemistry of the sulfone would be expected to maximize this resonance effect, the differences between the two systems are to great to permit an estimation of the effect of stereochemistry.

The negative deviation of methyl dimethoxyacetate and methyl difluoroacetate from the Taft correlation can be explained in part by stabilization of the reacting ester by double bond - no bond resonance. The stabilizing effect of two oxygen atoms or two fluorine atoms attached to an unsaturated carbon is reported (8) to be about 7.0 and 6.5 kcal/mole respectively. The degree to which this resonance is responsible for the negative deviations from the Taft correlations depends upon the fraction of this resonance maintained in the transition state. A full effect (i.e. no resonance in the transition state) for methyl dimethoxyacetate would require a correction in log k of 7.0/2.3 RT or 5.0 log units. A full effect for methyl difluoroacetate would be 4.6 log units. A maximum correction for the effects of double bond - no bond resonance in the disubstituted esters (assuming the correctness of the values cited for this resonance) still results in a negative deviation from the Taft correlation. This, of course, is in

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37. S. Andreades, J. Am. Chem. Soc., 86, 2003 (1964).

38. J. Hine and O. B. Ramsay, J. Am. Chem. Soc., 84, 973 (1962).

agreement with the predication of hybridization effects. The required negative deviation is also observed for methyl fluoroacetate and methyl methoxyacetate.

Electronegativity Correlation of Rates

Earlier it was postulated that reactions involving substituents attached to carbon undergoing a change in hybridization might be expected, when resonance and steric effects are constant, to conform to the relation.

$$\log \frac{k}{k_o} = \rho^* \sigma^* + \rho^H \sigma^H \qquad (8)$$

In this equation $\rho^H = 46D^{\ddagger}/2.3RT$, $\sigma^H = X - X_o$, and the change in the electronegativity of carbon on going to the transition state is equal to $D^{\ddagger}$. This linear free energy relationship, Equation 8, has three terms: the first correlates the polar effect of a substituent upon the rate: the second correlates the hybridization effect upon the rate in terms of the electronegativity of the bonding atom of the substituent: the third is log k of the standard compound.

The polar effect on the methoxide-catalyzed deuterium exchange of alpha substituted methyl acetates has been correlated by the Taft relation, Equation 7, in which the standard compound would be methyl

$$\log k^* = 1.79(\sigma_X^* + \sigma_Y^*) - 4.604 \qquad (9)$$

isobutyrate, and k^* is the rate expected from a consideration of polar effects only. Assuming that the effects of resonance have been accounted for, deviations from this equation, Table 5, can be equated to $\rho^H\sigma^H$ where σ^H is defined by $X_X + X_Y - 2X_C$ or $X_X + X_Y - 5.0$.

$$\rho^H(X_X + X_Y - 5.0) = \log k - 1.79(\sigma_X^* + \sigma_Y^*) + 4.604 \qquad (10)$$

This function is plotted in Figure 6 for all the esters excepting methyl phenylacetate and methyl 3-methoxypropionate whose deviations from the Taft plot have already been discussed. The points for the four compounds in which a substituent is attached through a carbon atom almost coincided and are labeled $C\text{-}CH_2CO_2CH_3$ collectively. The best straight line has been drawn through the points for the monosubstituted acetates, neglecting the disubstituted acetates for reasons that will be discussed later. The slope of this line is -2.4 and is equal to ρ^H. From this, the value of $D^{\ddagger}$ is thus 0.073 units. This value does not appear to be unreasonable. Gordy (5) estimated that sp carbon is 0.28 units more electronegative than sp^3 carbon. If a linear relationship exists between per cent s character and electronegativity, sp^2 carbon should be about 0.093 units more electronegative than sp^3 carbon. In the transition state for formation of carbanions from the substituted acetates of the present study, the hybridization of the alpha carbon atom changes from sp^3 almost, but not entirely to sp^2. The observed value of $D^{\ddagger}$, 0.073, is what might be expected if the transition state occured at 80 per cent carbanion formation.

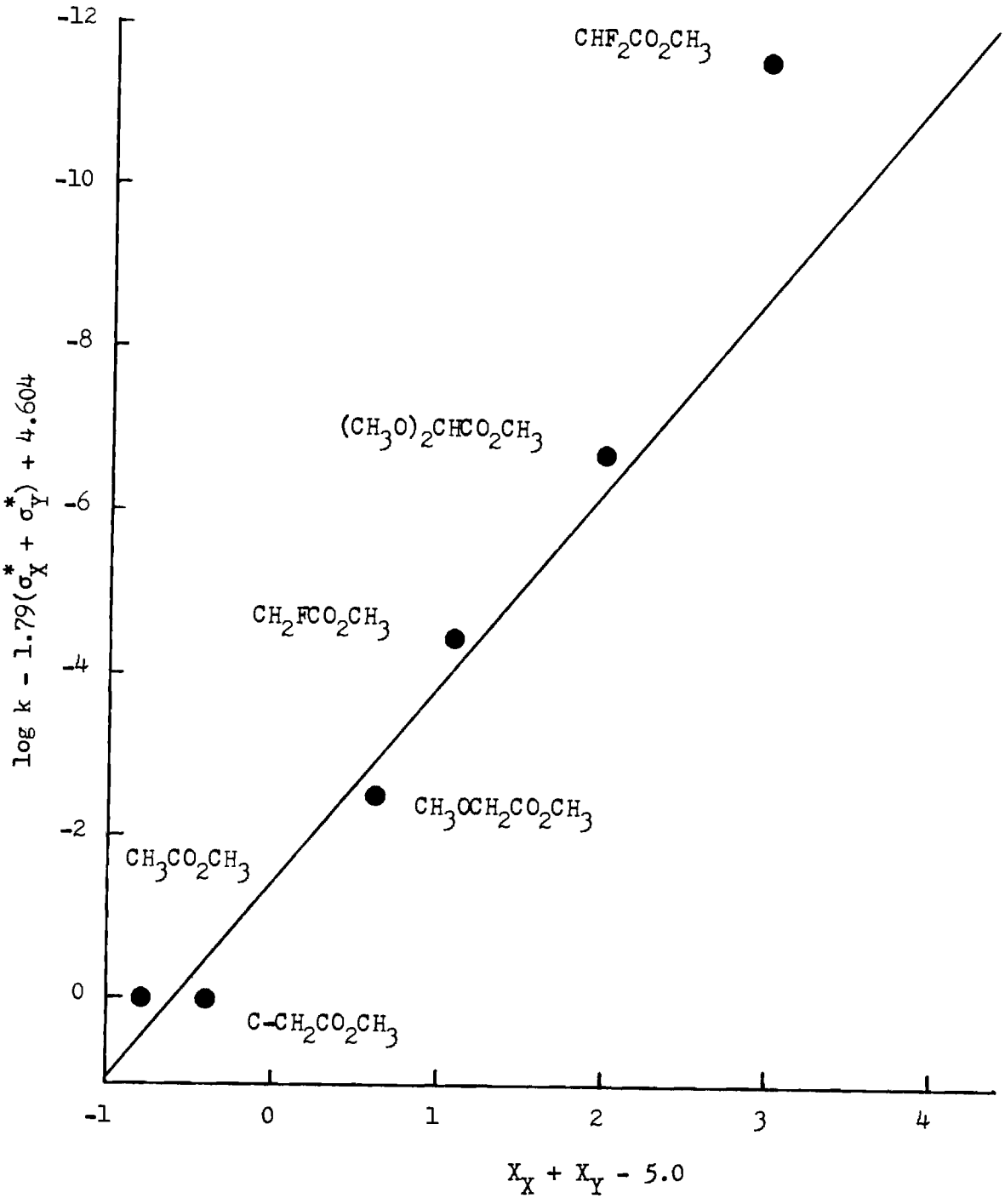

Figure 6. Correlation of Electronegativity and Rate for the Esters $XYCHCO_2CH_3$

Estimates of sigma-orbital electronegativities have been made for hybridized carbon by Hinze and Jaffe (39) which are not in accord with those of the present study or those of Gordy (5). On the Pauling scale, the sigma-orbital electronegativities of $\underline{sp}^3$, $\underline{sp}^2$, and $\underline{sp}$ carbon were estimated to be 2.48, 2.75, and 3.29 respectively.

It might have been thought that the effect of the electronegativities of the bonding atoms of substituents X and Y would be accounted for by the values of σ_X^* and σ_Y^*. Sager and Ritchie, (40) for example, have shown that linear free energy relationships of the form of the Taft and Hammett equations can be derived in which the substituent constants become group electronegativities. However, there seem to be discrepancies between σ^* values and group electronegativities. The charge separation in an H-X bond correlates well with the differences in electronegativity of H and X, but when a C-X ($\underline{sp}^3$ carbon) bond is considered the agreement is far from quantitative (3). In fact, the bond moment in methane, $u_{C^+H^-} = 0.30D$ (41), suggests that the electronegativity of H is greater than that of $\underline{sp}^3$ carbon as is indicated by Moffitt's electronegativities (42). Also the Pauling electronegativities stand in the order O > Cl > C = I while the values of σ^* for the corresponding XCH_2 (or $HXCH_2$ or H_3XCH_2) groups stand in the order Cl > I > O > C. In view of certain uncertainties regarding

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39. J. Hinze and H. H. Jaffe, J. Am. Chem. Soc., 84, 540 (1962).

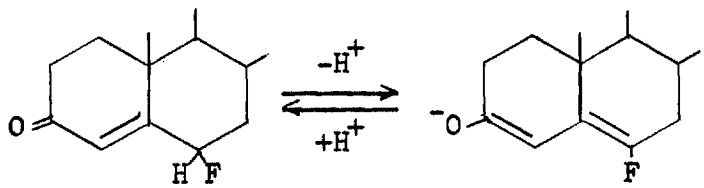
40. W. F. Sager and C. D. Ritchie, ibid., 83, 3498 (1961).

41. C. R. Mueller and H. Eyring, J. Chem. Phys., 19, 193 (1951).

42. W. Moffitt, Proc. Roy. Soc. (London), A202, 548 (1950).

electronegativity values, and in some cases the relative order, we feel that the correlation between rate and electronegativity has been moderately successful for the monosubstituted acetates.

Recently Subrahmanyan, Malhotra, and Ringold (43) have reported that both axial and equatorial 4-fluoro substituents in androst -4-ene-3,17-dione increase the equilibrium constant for the removal of 4-protons by potassium tert-butoxide. This activating effect of axial and equatorial fluorine relative to hydrogen, 13-fold and 90-fold, was attributed to the inductive effect and to resonance interaction of the fluorine atom with the conjugated pi system. It was noted that such



resonance may be encouraged by the existence of the carbanion as an ion-pair and by the large size of the pi system, which could more easily accomodate additional negative charge. At present it is difficult to compare the effect of fluorine in this case with that observed in fluoroacetate, however, further studies of the steriod system in ion dissociating solvents have been promised.

It was mentioned earlier that the attachment of two fluorine atoms or two alkoxy groups to the same saturated carbon atom results in

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43. G. Subrahmanyan, S. K. Malhotra, and H. J. Ringold, J. Am. Chem. Soc., 88, 1332 (1966).

a net stabilization of about 6.5 and 7.0 kcal/mole. If, for instance, this stabilization is 80 per cent lost in the transition state for carbanion formation, log k would be decreased by 3.7. A correction for this effect would move the point for methyl difluoroacetate in Figure 6 to about 0.8 log units above the line. A corresponding correction for methyl dimethoxyacetate would move log k for this compound 3.5 log units below the line. It seems reasonable that a correction is warranted for both compounds, although the extent to which it should be made is questionable. Hence, the position of log k for methyl difluoroacetate in Figure 6 is not unreasonable with regard to the line, but methyl dimethoxy appears to be about 3 powers of ten more reactive than might have been expected. Perhaps the strongly resonance-electron-donating methoxy groups are capable of stabilizing the transition state for formation of the enolate anion by donating electrons to the pi system. This relationization is qualitatively consistent with the progressive downward deviation of alkoxyacetates from the line, Figure 6, as alkoxy substitution is increased.

CHAPTER IV

CONCLUSION

The study of the deuterium exchange of substituted methyl acetates presented in this work was undertaken in order to verify a novel substituent effect which was postulated to arise from the interaction of highly electronegative atoms and a bound carbon atom which is undergoing a change in hybridization during a reaction. This methoxide catalyzed deuterium exchange reaction was shown to obey the Taft relation, for some substituents, with fair precision. The deviation of methyl 3-methoxypropionate raises an interesting possible example of double bond - no bond resonance which warrants further study. Deviations of fluoroacetate and methoxyacetate were correlated successfully in terms of the hybridization effect postulated; these deviations are as large as a factor of four powers of ten. Difluoroacetate was also correlated after a correction was applied for double bond - no bond resonance. Dimethoxyacetate was found to be about three powers of ten more reactive than predicted when a correction was made for double bond - no bond resonance. An estimation of the difference in the electronegativity of $\underline{sp}^2$ and $\underline{sp}^3$ carbon was made in which $\underline{sp}^2$ carbon is greater by 0.073 electronegativity units on the Pauling scale.

A consideration of data available in the literature strongly indicates the hybridization effect but quantitative evaluation was not possible without further information.

APPENDIX

Table 4. Summary of Deuterium Exchange Kinetic Data at 35°

Ester	Table No.	$[NaOCH_3]$	k ($M^{-1}sec^{-1}$)
Methyl Acetate	6	0.0972	1.24×10^{-3}
	7	0.0511	1.32×10^{-3}
		0.0621	1.21×10^{-3}[a]
Methyl Propionate	8	0.306	1.65×10^{-4}
	9	0.172	1.63×10^{-4}
Methyl Butyrate	10	0.579	1.22×10^{-4}
	11	0.315	1.29×10^{-4}
		0.295	1.35×10^{-4}[a]
Methyl 3-Methoxypropionate	12	0.0103	2.50×10^{-2}
	13	0.00989	2.68×10^{-2}
Dimethyl Succinate	14	0.0431	3.63×10^{-3}
	15	0.0264	3.40×10^{-3}
		0.0655	3.70×10^{-3}[a]
Methyl Hydrocinnamate	16	0.203	5.72×10^{-4}
	17	0.284	5.35×10^{-4}
Methyl Methoxyacetate	18	0.1045	9.36×10^{-4}
	19	0.0882	9.12×10^{-4}
Methyl Dimethoxyacetate	20	0.644	1.4×10^{-5}
	21	0.634	1.11×10^{-5}
Methyl Fluoroacetate	22	0.0944	2.27×10^{-3}
	23	0.0922	2.30×10^{-3}
Methyl Difluoroacetate	24	0.362	7.6×10^{-6}
	25	0.560	7.50×10^{-6}
Methyl Phenylacetate	26	0.0043	4.1×10^{-1}

[a]Runs by C. L. Liotta

Table 5. Taft Correlation of Rate Constants for the Esters $XYCHCO_2CH_3$

Ester	k ($\underline{M}^{-1}sec^{-1}$)	-log k	$(\sigma_X^* + \sigma_Y^*)^a$	-log k^*	log $\frac{k}{k^*}$
$CH_3CO_2CH_3$	1.26×10^{-3}	2.900	0.98	2.850	-0.050
$CH_3CH_2CO_2CH_3$	1.64×10^{-4}	3.785	0.49	3.727	-0.058
$CH_3CH_2CH_2CO_2CH_3$	1.29×10^{-4}	3.889	0.39	3.906	0.017
$CH_3OCH_2CH_2CO_2CH_3$	2.59×10^{-2}	1.587	1.13	2.558	0.973
$(-CH_2CO_2CH_3)$	3.58×10^{-3}	2.446	1.20[b]	2.456	0.010
$PhCH_2CH_2CO_2CH_3$	5.53×10^{-4}	3.259	0.71	3.333	0.074
$CH_3OCH_2CO_2CH_3$	9.24×10^{-4}	3.034	2.28[b]	0.524	-2.510
$(CH_3O)_2CHCO_2CH_3$	1.25×10^{-5}	4.903	3.58[b]	-1.803	-6.706
$FCH_2CO_2CH_3$	2.28×10^{-3}	2.642	3.57[b]	-1.786	-4.428
$F_2CHCO_2CH_3$	7.55×10^{-6}	5.122	6.16[b]	-6.441	-11.563
$PhCH_2CO_2CH_3$	$> 4.1 \times 10^{-1}$	< 0.40	1.09	2.654	2.256

[a]Sigma values are taken from reference 34.

[b]Using the relation $\sigma_X^* \approx 2.8\ \sigma_{CH_2X}^*$

Table 6. Deuterium Exchange of Methyl Acetate--0.0972 M Sodium Methoxide

0.429 M Methyl Acetate $[CH_3OH]_o = 0.379$

Time (Seconds)	A (obs)	l (cm)	A	Log $\frac{A_\infty - A_o}{A_\infty - A}$
		0.00550		
197	0.313		0.567	0.012
663	0.368		0.665	0.035
977	0.403		0.727	0.051
1283	0.452		0.813	0.073
1695	0.484		0.868	0.087
2000	0.520		0.932	0.105
2333	0.550	0.00561	0.982	0.120
2929	0.613		1.090	0.153
3290	0.653		1.156	0.175
3772	0.693		1.226	0.199
4190	0.727		1.281	0.219
4975	0.786		1.380	0.258
5725	0.847	0.00571	1.481	0.301
6718	0.882		1.542	0.329
9020	1.08		1.88	0.534

$$k = 1.24 \times 10^{-3}\ \underline{M}^{-1}\ sec^{-1}$$

Table 7. Deuterium Exchange of Methyl Acetate--0.0511 M Sodium Methoxide

0.1879 M Methyl Acetate $[CH_3OH]_o = 0.383$

Time (Seconds)	A (obs)	l (cm)	A	Log A
144	0.309	0.00579	0.531	0.001
719	0.328		0.561	0.019
1672	0.352		0.600	0.043
4300	0.429		0.729	0.135
5275	0.442		0.749	0.151
6350	0.463		0.781	0.178
8210	0.501		0.840	0.235
10690	0.557		0.929	0.334
15966	0.643		1.070	0.565
		0.00604		

$$k = 1.32 \times 10^{-3}\ \underline{M}^{-1}\ sec^{-1}$$

Table 8. Deuterium Exchange of Methyl Propionate--0.306 M Sodium Methoxide

0.990 M Methyl Propionate $[CH_3OH]_o = 0.428$

Time (Seconds)	A (obs)	l (cm)	A	Log $\frac{A_\infty - A_o}{A_\infty - A}$
		0.00547		
121	0.312		0.575	0.000
721	0.364		0.667	0.017
1790	0.434	0.00540	0.800	0.042
3222	0.521		0.954	0.074
4131	0.564		1.032	0.092
5600	0.645		1.180	0.126
6466	0.689	0.00554	1.255	0.145
7820	0.749		1.365	0.174
8890	0.777		1.415	0.187
9837	0.813		1.472	0.204
10750	0.864		1.565	0.235
19000	1.10	0.00550	1.99	0.390

$$k = 1.65 \times 10^{-4}\ \underline{M}^{-1}\ sec^{-1}$$

Table 9. Deuterium Exchange of Methyl Propionate--0.172 M Sodium Methoxide

0.421 M Methyl Propionate $[CH_3OH]_o = 0.425$

Time (Seconds)	A (obs)	l (cm)	A	Log $\frac{A_\infty - A_o}{A_\infty - A}$
		0.00574		
118	0.329		0.572	0.0006
844	0.339		0.586	0.0068
1579	0.348		0.600	0.0123
2397	0.361		0.620	0.0208
3754	0.390	0.00584	0.668	0.0418
4510	0.405		0.691	0.0524
6037	0.436		0.740	0.0751
6975	0.454		0.758	0.0840
		0.00603		
9766	0.491		0.818	0.1147
12290	0.529		0.876	0.1457
13950	0.556		0.918	0.1700
17406	0.595		0.976	0.2076

$k = 1.63 \times 10^{-4}\ M^{-1}\ sec^{-1}$

[a]Five other analysis on the kinetics of methyl methoxyacetate, Table 18, were made as is indicated by blank spaces. The base concentration of both runs are comparable.

Table 10. Deuterium Exchange of Methyl Butyrate--0.579 M Sodium Methoxide

0.380 M Methyl Butyrate $[CH_3OH]_o = 0.355$

Time (Seconds)	A (obs)	l (cm)	A	Log $\frac{A_\infty - A_o}{A_\infty - A}$
		0.00603		
962	0.322		0.534	0.035
1822	0.370		0.614	0.076
2163	0.368		0.609	0.073
2600	0.398		0.657	0.100
3020	0.402	0.00607	0.663	0.103
3800	0.425		0.700	0.125
4200	0.448		0.736	0.148
4600	0.446		0.734	0.146
7811	0.530		0.869	0.242
8737	0.557		0.912	0.277
9151	0.563		0.921	0.285
14620	0.665		1.087	0.462
15480	0.672		1.099	0.478
16328	0.693	0.00613	1.131	0.523

$$k = 1.22 \times 10^{-4}\ \underline{M}^{-1}\ sec^{-1}$$

Table 11. Deuterium Exchange of Methyl Butyrate--0.315 M Sodium Methoxide

0.325 M Methyl Butyrate $[CH_3OH]_o = 0.424$

Time (Seconds)	A (obs)	l (cm)	A	Log $\frac{A_\infty - A_o}{A_\infty - A}$
200	0.322	0.00568	0.564	0.000
660	0.332		0.582	0.009
1100	0.349		0.614	0.027
1600	0.356		0.626	0.034
2208	0.362		0.635	0.038
3580	0.392		0.688	0.070
5655	0.420		0.740	0.103
6966	0.435		0.766	0.120
9500	0.466		0.820	0.159
11250	0.490		0.863	0.193
21230	0.596		1.049	0.378
27480	0.647	0.00568	1.140	0.510

$$k = 1.29 \times 10^{-4}\ \underline{M}^{-1}\ sec^{-1}$$

Table 12. Deuterium Exchange of Methyl 3-Methoxypropionate--0.0103 M Sodium Methoxide

0.514 M Methyl 3-Methoxypropionate $[CH_3OH]_o = 0.462$

Time (Seconds)	A (obs)	l (cm)	A	Log $\frac{A_\infty - A_o}{A_\infty - A}$
		0.00624		
100	0.419		0.663	0.010
720	0.535		0.840	0.074
1280	0.637		0.991	0.137
1830	0.740		1.137	0.208
2240	0.780		1.186	0.234
2930	0.883		1.330	0.324
7035	1.140	0.00671	1.70	0.708

$k = 2.50 \times 10^{-2}\ M^{-1}\ sec^{-1}$

Table 13. Deuterium Exchange of Methyl 3-Methoxypropionate--0.00989 M Sodium Methoxide

0.2065 M Methyl 3-Methoxypropionate $[CH_3OH]_o = 0.406$

Time (Seconds)	A (obs)	l (cm)	A	Log $\frac{A_\infty - A_o}{A_\infty - A}$
85	0.289	0.00514	0.558	0.002
568	0.330		0.634	0.067
1133	0.365		0.698	0.131
1897	0.410		0.782	0.232
3204	0.457	0.00527	0.868	0.367
5100	0.515		0.973	0.624
6660	0.528		0.994	0.700
10020	0.569		1.063	1.135

$k = 2.68 \times 10^{-2}\ M^{-1}\ sec^{-1}$

Table 14. Deuterium Exchange of Dimethyl Succinate--0.0431 M Sodium Methoxide

0.210 M Dimethyl Succinate $[CH_3OH]_o = 0.365$

Time (Seconds)	A (obs)	l (cm)	A	Log $\frac{A_\infty - A_o}{A_\infty - A}$
		0.00657		
105	0.366		0.556	0.023
408	0.406		0.614	0.048
820	0.433		0.654	0.066
1130	0.459		0.690	0.083
1432	0.493		0.740	0.108
2030	0.547		0.818	0.149
3166	0.622		0.927	0.215
3500	0.655	0.00674	0.972	0.245
4300	0.708		1.047	0.300
4650	0.734		1.081	0.328
5500	0.780		1.148	0.389
6760	0.839		1.232	0.479
8142	0.887		1.296	0.563
9820	0.976	0.00687	1.420	0.794

$$k = 3.63 \times 10^{-3}\ \underline{M}^{-1}\ sec^{-1}$$

Table 15. Deuterium Exchange of Dimethyl Succinate--0.0264 M Sodium Methoxide

0.256 M Dimethyl Succinate $[CH_3OH]_o = 0.400$

Time (Seconds)	A (obs)	l (cm)	A	Log $\frac{A_\infty - A_o}{A_\infty - A}$
		0.00687		
216	0.391		0.566	0.006
675	0.421		0.608	0.020
984	0.447		0.642	0.032
1400	0.479		0.684	0.047
1925	0.518		0.736	0.066
2390	0.549		0.778	0.083
3640	0.638		0.900	0.134
3995	0.661		0.938	0.147
5232	0.744	0.00715	0.030	0.196
6100	0.785		1.091	0.229
7000	0.834		1.154	0.265
8175	0.877		1.209	0.300
9580	0.935	0.00729	1.282	0.350

$$k = 3.40 \times 10^{-3}\ \underline{M}^{-1}\ sec^{-1}$$

Table 16. Deuterium Exchange of Methyl Hydrocinnamate--0.203 M Sodium Methoxide

0.518 M Methyl Hydrocinnamate $[CH_3OH]_o = 0.365$

Time (Seconds)	A (obs)	l (cm)	A	Log $\frac{A\infty - Ao}{A\infty - Ao}$
		0.00729		
163	0.380		0.520	0.009
676	0.443		0.606	0.038
1060	0.482		0.659	0.058
1470	0.527		0.718	0.080
2557	0.628		0.856	0.138
3250	0.688		0.936	0.175
3580	0.728		0.989	0.202
4775	0.803	0.0734	1.090	0.258
6048	0.850		1.152	0.296
6048	0.756	0.00648[a]	1.169	0.305
7525	0.823		1.272	0.382
8107	0.845		1.306	0.409
8571	0.860		1.330	0.430
10090	0.912	0.00646	1.410	0.506

$$k = 5.72 \times 10^{-4}\ \underline{M}^{-1}\ sec^{-1}$$

[a]New cell used for this and following analyses.

Table 17. Deuterium Exchange of Methyl Hydrocinnamate--0.284 M Sodium Methoxide

0.894 M Methyl Hydrocinnamate $[CH_3OH]_o = 0.369$

Time (Seconds)	A (obs)	l (cm)	A	Log $\frac{A_\infty - A_o}{A_\infty - A}$
122	0.293	0.00552	0.530	0.007
485	0.358		0.644	0.031
900	0.433		0.776	0.060
1152	0.476		0.848	0.076
1445	0.526		0.933	0.097
1906	0.593		1.046	0.126
3000	0.734	0.00572	1.288	0.195
3900	0.829		1.446	0.247
5000	0.920		1.598	0.303
6250	1.06		1.83	0.407
7410	1.12	0.00580	1.93	0.461

$$k = 5.34 \times 10^{-4}\ \underline{M}^{-1}\ sec^{-1}$$

Table 18. Deuterium Exchange of Methyl Methoxyacetate--0.1045 M Sodium Methoxide

0.809 M Methyl Methoxyacetate $[CH_3OH]_o = 0.406$

Time (Seconds)	A (obs)	l (cm)[a]	A	Log $\frac{A_\infty - A_o}{A_\infty - A}$
165	0.405	0.00588	0.689	0.0088
769	0.477	0.00592	0.806	0.0356
1108	0.518	0.00594	0.873	0.0517
2088	0.612	0.00598	1.022	0.0899
4505	0.823	0.00603	1.365	0.1932

$$k = 9.36 \times 10^{-4}\ M^{-1}\ sec^{-1}$$

[a]Values are interpolated from data of Table 9.

Table 19. Deuterium Exchange of Methyl Methoxyacetate--0.0882 M Sodium Methoxide

0.649 M Methyl Methoxyacetate $[CH_3OH]_o = 0.396$

Time (Seconds)	A (obs)	l (cm)	A	Log $\frac{A_\infty - A_o}{A_\infty - A}$
1222	0.435	0.00613	0.706	0.047
1547	0.460		0.742	0.057
1944	0.490		0.788	0.071
2262	0.514		0.822	0.082
2707	0.551		0.878	0.100
3327	0.598		0.948	0.124
3725	0.618		0.976	0.134
4111	0.649		1.018	0.145
4590	0.681		1.064	0.167
5021	0.710	0.00642	1.106	0.183
6354	0.778		1.206	0.225
8170	0.865		1.335	0.286
8460	0.879		1.351	0.295
8910	0.905		1.385	0.312
9250	0.921		1.402	0.322
9537	0.925		1.401	0.311

$$k = 9.12 \times 10^{-4}\ \underline{M}^{-1}\ sec^{-1}$$

Table 20. Deuterium Exchange of Methyl Dimethoxyacetate--0.644 M Sodium Methoxide

0.922 M Methyl Dimethoxyacetate $[CH_3OH]_o = 0.304$

Time (Seconds)	A (obs)	l (cm)	A	Log $\frac{A_\infty - A_o}{A_\infty - A}$
330	0.262	0.00660	0.397	0.0006
1030	0.272		0.414	0.0070
1557	0.270		0.411	0.0053
3550	0.291		0.442	0.0178
4836	0.292		0.444	0.0184
9250	0.328		0.499	0.0408
9800	0.329		0.500	0.0414
10540	0.333		0.506	0.0439
16254	0.365		0.555	0.0650
16747	0.367		0.588	0.0664
23153	0.405		0.616	0.0929
24910	0.415		0.631	0.1001
25218	0.416		0.633	0.1009
30734	0.442		0.672	0.1203
31111	0.445	0.0657	0.677	0.1226

$$k = 1.4 \times 10^{-5}\ \underline{M}^{-1}\ sec^{-1}$$

Table 21. Deuterium Exchange of Methyl Dimethoxyacetate--0.634 M Sodium Methoxide

0.952 M Methyl Dimethoxyacetate $[CH_3OH]_o = 0.327$

Time (Hours)	A (obs)	l (cm)	A	Log $\frac{A_\infty - A_o}{A_\infty - A}$
0.0	0.264	0.00621	0.425	0.000
10.8	0.456		0.730	0.132
15.4	0.504		0.805	0.171
19.0	0.557		0.888	0.220
22.8	0.592		0.938	0.248
36.5	0.713		1.125	0.399
41.1	0.760	0.00636	1.195	0.470
47.2	0.782		1.225	0.504

$$k = 1.11 \times 10^{-5}\ \underline{M}^{-1}\ sec^{-1}$$

Table 22. Deuterium Exchange of Methyl Fluoroacetate--0.0944 M Sodium Methoxide

0.403 M Methyl Fluoroacetate $[CH_3OH]_o = 0.418$

Time (Seconds)	A (obs)	l (cm)	A	Log $\frac{A_\infty - A_o}{A_\infty - A}$
324	0.359	0.00581	0.615	0.020
750	0.405		0.692	0.055
1230	0.454		0.775	0.096
1700	0.502		0.854	0.139
2080	0.542		0.918	0.177
2535	0.573		0.968	0.209
3006	0.611		1.029	0.253
3858	0.677		1.139	0.343
4215	0.704		1.180	0.382
5730	0.773		1.295	0.517
6850	0.827	0.00599	1.383	0.657

$$k = 2.27 \times 10^{-3}\ \underline{M}^{-1}\ sec^{-1}$$

Table 23. Deuterium Exchange of Methyl Fluoroacetate--0.0922 M Sodium Methoxide

0.399 M Methyl Fluoroacetate $[CH_3OH]_o = 0.410$

Time (Seconds)	A (obs)	l (cm)	A	Log $\frac{A_\infty - A_o}{A_\infty - A}$
		0.00599		
185	0.356		0.594	0.015
675	0.412		0.684	0.056
990	0.455		0.754	0.091
1971	9.551		0.909	0.179
2293	0.573		0.943	0.201
2595	0.605		0.991	0.235
3658	0.692		1.132	0.350
3966	0.702		1.143	0.361
4360	0.735		1.194	0.413
5550	0.785		1.270	0.505
6410	0.825		1.331	0.585
7445	0.853	0.00621	1.374	0.673

$$k = 2.30 \times 10^{-3}\ \underline{M}^{-1}\ sec^{-1}$$

Table 24. Deuterium Exchange of Methyl Difluoroacetate--0.362 M Sodium Methoxide

0.256 M Methyl Difluoroacetate $[CH_3OH]_o = 0.422$

Time (Hours)	A (obs)	l (cm)	A	Log $\frac{A_\infty - A_o}{A_\infty - A}$
0.00	0.312	0.00560	0.557	0.004
3.75	0.310		0.553	0.001
7.57	0.341		0.608	0.078
11.78	0.337		0.602	0.069
15.97	0.325		0.580	0.036
19.53	0.349		0.623	0.102
24.00	0.350		0.624	0.104
52.67	0.399	0.00560[a]	0.712	0.283
67.12	0.424	0.00580	0.731	0.334
94.47	0.431		0.741	0.370
176.00	0.476	0.00580	0.821	0.719

$$k = 7.6 \times 10^{-6}\ \underline{M}^{-1}\ sec^{-1}$$

[a]Other analyses were made prior to this measurement.

Table 25. Deuterium Exchange of Methyl Difluoroacetate--0.560 M Sodium Methoxide

1.085 M Methyl Difluoroacetate $[CH_3OH]_o = 0.311$

Time (Hours)	A (obs)	l (cm)	A	Log $\frac{A_\infty - A_o}{A_\infty - A}$
0.0	0.253	0.00621	0.408	0.000
10.6	0.407		0.652	0.088
15.2	0.447		0.713	0.113
19.1	0.483		0.768	0.136
22.9	0.518		0.821	0.161
36.6	0.632		0.997	0.253
41.4	0.670	0.00636	1.053	0.287
46.7	0.713		1.116	0.328

$$k = 7.50 \times 10^{-6}\ \underline{M}^{-1}\ sec^{-1}$$

Table 26. Deuterium Exchange of Methyl Phenylacetate--0.0043 M Sodium Methoxide

0.563 M Methyl Phenylacetate $[CH_3OH]_o = 0.400$

Time (Seconds)	A (obs)	l (cm)	A	Log $\frac{A_\infty - A_o}{A_\infty - A}$
		0.00514		
60	.475		.918	0.127
430	.740		1.424	0.401
666	.851		1.626	0.588
930	.930	0.00526	1.768	0.796

$$k = 4.1 \times 10^{-1}\ M^{-1}\ sec^{-1}$$

Table 27. Rough Deuterium Exchange of Methyl 3-Ethoxypropionate

0.31 M Ester — l = 0.0064 cm.

0.40 M Sodium Methoxide — T ≈ 30 - 35°

Time (Seconds)	$A - A_o$
0	0.048
55	0.086
110	0.125
165	0.159
220	0.189
275	0.217
330	0.245
385	0.268
440	0.289
495	0.307
550	0.327
605	0.347
660	0.363
715	0.378
825	0.402
935	0.422
1045	0.439
1155	0.453
1265	0.461
∞[a]	0.484

$t_{1/2} \approx 350$ sec.

$k \approx 5 \times 10^{-3}\ M^{-1}\ sec^{-1}$

[a]Projected value. Calculated value is ca. 0.52.

Table 28. Kinetics of the Drying of Methanol at 64.5°

0.200 M Dimethyl Phthalate 0.189 M Water

Time (Seconds)	[Base]	$\frac{k K t}{24}$
0	0.1598	0.0
2400	0.1316	8.5
6900	0.1030	18.8
9780	0.0889	26.0
15300	0.0722	42.1
16200	0.0721	42.2
74400	0.0235	245

$$k K = 6.0 \times 10^{-2} \text{ M}^{-2} \text{ sec}^{-1}$$

Table 29. Density of Sodium Methoxide-Methanol and Sodium Methoxide-Methanol-O-d Solutions at 25°

$[NaOCH_3]$	Density (g./ml.)	
	Methanol Solution	Methanol-O-d Solution[a]
0.000	0.786	.810
0.305	0.802	.826
0.598	0.815	.839
1.175	0.840	.863
2.327	0.881	.904

[a]Calculated from data for methanol solutions assuming identical partial molar volumes for methanol and methanol-O-d.

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PART TWO

CHAPTER I

INTRODUCTION

Using Pauling's defining equation for electronegativity and the principle that the electronegativity of carbon increases with its degree of unsaturation, an equation can be derived which predicts destabilization of olefins having highly electronegative atoms bound to unsaturated carbon[1]. The purpose of this work is to determine the effect of alkoxy and thioalkoxy groups upon the stability of certain unsaturated compounds in order to investigate this electronegativity effect.

The literature contains many examples of base-catalyzed rearrangements of allyl ethers which indicate that alkoxy groups stabilize double bonds more than hydrogen does. Allyl vinyl ether is converted to propenyl vinyl ether by the action of sodium amide in liquid ammonia (1, 2), 3-butoxy-2-methylpropene is similarly converted into 1-butoxy-2-methylpropene (3). Potassium tert-butoxide converts 2,5-dihydrofuran

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[1] See part one of this work for further discussion.

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(4). Moreover, it has been recently discovered that the steric course of this type of rearrangement is to give almost exclusively cis-propenyl ethers (5, 6). Compounds found to give cis-propenyl ethers in high yield are 1,4-diallyloxybutane, 1,5-diallyloxypentane, 4-allyloxybutanol, and the tetra-allyl ether of pentaerythritol. Under basic conditions sufficient to isomerize 2,5-dihydrofuran, 3-n-propoxycyclohexene does not isomerize, in the required trans fashion, to 1-n-propoxycyclohexene (1). The reason for the cis-stereospecificity is not known, but the subject has received some discussion (6, 7).

Thioalkoxy groups show an ability to stabilize olefins similar to that of alkoxy groups. During an investigation of the Claisen rearrangement, Tarbell and co-workers (8) found several examples of base-catalyzed isomerizations of allyl aryl thioethers to aryl propenyl thioethers. The activating influence of the sulfur atom is such that these isomerizations can be effected with less basic conditions than those required for the oxygen analogues. Furthermore, Price and Snyder (9) found both cis and trans propenyl sulfides are obtained from a number of alkyl allyl

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sulfides. O'Connor and co-workers (10) have investigated the equilibria between allyl and propenyl sulfides, sulfoxides, and sulfones. Their results are presented in Table 1. O'Connor pointed out that stablization

Table 1. Composition of Equilibrium Mixture for Unsaturated Sulfides, Sulfoxides, and Sulfones (11).

$$RCH_2CH{=}CHX \underset{\text{Base}}{\overset{K}{\rightleftharpoons}} RCH{=}CHCH_2X$$

R	X	K[a]
H	SCH_3	< 0.01
H	$SOCH_3$	0.25
H	SO_2CH_3	0.80
C_3H_7	SCH_3	0.5
C_3H_7	$SOCH_3$	24
CH_3	$SOCH_3$	32
C_3H_7	SO_2CH_3	> 99

[a] No distinction between cis and trans isomers.

effects due to sulfur-electron-pair delocalization into the double bond are found to decrease in the order $CH_3S > CH_3SO > CH_3SO_2$ as expected; but this does not explain the fact that $CH_3SO_2CH_2 > CH_3SO_2$ and $CH_3SOCH_2 > CH_3SO$ in ability to stabilize the respective olefins. The latter

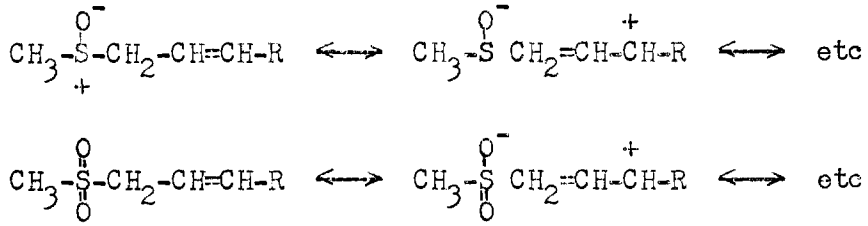
10. D. E. O'Connor and W. I. Lyness, J. Am. Chem. Soc., 85, 3045 (1963); D. E. O'Connor and C. D. Broaddus, ibid., 86, 2267 (1964); D. E. O'Connor and W. I. Lyness, ibid., 86, 3840 (1964).

11. D. J. Cram, "Fundamentals of Carbanion Chemsitry," Academic Press, New York, 1965, p. 203.

order was rationalized in terms of a inductive destabilization of the olefins by CH_3SO_2 and CH_3SO. Cram offered an explanation for this effect.

> Groups that possess strong electron-withdrawing properties tend to form bonds to carbon which are richest in p-character, since p-orbitals are more extended than s-orbitals. The vinyl group forms bonds with sp^2 and the allyl with sp^3 orbitals, the latter being richer in p-character. Thus the inductive effect seems mainly responsible for the position of equilibria in these olefins, with electron pair-pi interactions superimposed (11).

Cram's hypothesis is a possible alternative explanation of all the available data which the electronegativity effect seeks to explain. However, the observed order $CH_3SO_2CH_2 > CH_3SO_2$ and $CH_3SOCH_2 > CH_3SO$ in ability to stabilize the respective olefins might be due, in part, to an allylic resonance in which the sulfone or sulfoxide group is non-bonded. The greater dispersal of negative charge in the sulfone



would make $CH_3SO_2CH_2 > CH_3SOCH_2$ in ability to stabilize olefins; this is tantamount to the order above if the sulfoxide and sulfone groups are "neutral". The observation that 2,3-dihydrothiophene-1,1-dioxide is about as stable as 2,5-dihydrothiophene-1,1-dioxide (12) is consistent

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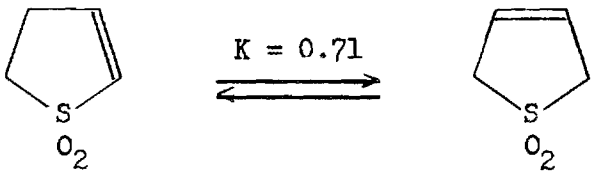
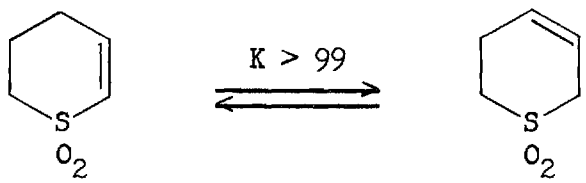
12. H. Zimmermannova and M. Prochazka, Coll. Czechoslov. Chem. Comm., 30, 286, (1965).

with this argument. The geometry of 2,5-dihydrothiophene-1,1-dioxide



(1

minimizes allylic resonance, since the hydrogens of the methylene groups should be nearly perpendicular to the plane defined by the methylene carbons and the double bond. On the other hand, in the less constrained dihydrothiopyran-1,1-dioxide the beta-gamma-unsaturated isomer is greatly favored in the equilibrium mixture (13).



(2

Olefins which have suitable activating groups, such as CO_2R, CO_2H, and CN, undergo base-catalyzed prototropic rearrangements readily. The equilibria between alpha-beta and beta-gamma unsaturated isomers of carbonyl compounds have been intensively investigated and have been reviewed by Baker (14). These equilibria may be explained by the ability of alkyl groups to stabilize double bonds by hyperconjugation and the more powerful ability of groups such as CO_2^-, CO_2H, CO_2R, COR, and CN

13. E. A. Fehnel, J. Am. Chem. Soc., 74, 1569 (1952).

14. J. W. Baker, "Tauntomerism," Routledge, London, 1934, Chap. 9.

to stabilize them by resonance. A methoxy group has been included in these comparisons since the hydroxide-catalyzed isomerization of sodium 4-methoxy-2-butenoate produces 70 per cent sodium 4-methoxy-3-butenoate at equilibrium (15). This would make a methoxy group about equal to an ethyl group in its ability to stabilize double bonds, since the salt of hexenoic acid gives the 2- and 3-isomers in the ratio of 25:75 at equilibrium (16).

The heat of hydrogenation of ethyl vinyl ether (26.7 kcal/mole) is 6.1 kcal/mole lower than that of ethylene (17). The heat of hydrogenation of divinyl ether is 57.2 kcal/mole or 30.5 kcal/mole for the first double bond (17). This is only 2.3 kcal/mole less than that of ethylene and it seems to show that the resonance donation of the unshared electrons of the oxygen atom to one double bond greatly decreases its ability to donate additional electrons by resonance to another double bond. This effect becomes even more important in the case of vinyl acetate whose heat of hydrogenation is 31.1 kcal/mole (17). Perhaps such compounds as vinyl perchlorate, vinyl sulfate, vinyl benzenesulfonate, or even vinyl trifluoroacetate would have a higher heat of hydrogenation than ethylene.

The difference between the Hammett substituent constants of a meta and para substituent is largely due to the more efficient operation

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15. L. N. Owen and M. U. S. Sultanbawa, J. Chem. Soc., 3098 (1949).

16. R. P. Linstead and E. G. Noble, J. Chem. Soc., 614 (1934).

17. M. A. Dolliver, T. L. Gresham, G. B. Kistiakowsky, E. A. Smith, W. E. Vaughan, J. Am. Chem. Soc., 60, 440 (1938).

of the resonance effect from the para position (18). In the ionization of benzoic acid, resonance-electron donor groups in the para position stabilize the acid by means of resonance interaction with the carbonyl

group. If the difference $\sigma_{meta} - \sigma_{para}$ is used as a measure of such resonance, CH_3O is much better than CH_3S as a resonance-electron donor since the differences are 0.38 and 0.15 respectively (19).

Thus it appears that alkoxy groups and, to a lesser extent, thioalkoxy groups stabilize olefins by means of resonance conjugation of their unshared electron pairs with the π-electron system of the double bond, and this obscures any destabilization resulting from the electronegativity of oxygen and sulfur. However, if one could compare the relative stabilization effects of alkoxy and thioalkoxy groups upon olefins, it might be possible to observe the electronegativity effect. The equilibrium between 3-methoxy-1-methylthiopropene and 1-methoxy-3-methylthiopropene could be used to make such a comparison. The effect

$$CH_3SCH{=}CHCH_2OCH_3 \overset{K}{\rightleftharpoons} CH_3SCH_2CH{=}CHOCH_3 \qquad (3$$

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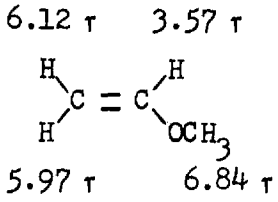
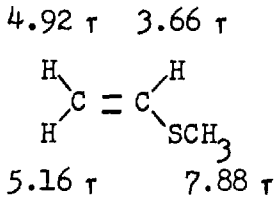
18. J. Hine, "Physical Organic Chemistry," 2nd ed., McGraw-Hill Book Co. Inc., New York, 1962, p. 92.

19. D. H. McDaniel and H. C. Brown, J. Org. Chem., 23, 420 (1958).

of any resonance stabilization of the double bond by CH_3O and CH_3S will tend to favor the vinyl ether at equilibrium. On the other hand, the electronegativity effect should offer a countering action since oxygen is more electronegative than sulfur. In the event that K is less than one, the electronegativity effect is well demonstrated; if greater than one, no unambiguous conclusion can be drawn.

A similar interplay of the relative differences in electronegativity and electron donation by resonance for oxygen and for sulfur is found in the n.m.r. spectra of methoxy vinyl ether and methylthio vinyl ether (20). The relative chemical shifts of the vinyl protons result from a unique combination of the deshielding effects of the oxygen and sulfur atoms. The protons <u>trans</u> to the methoxy and the





methylthio groups have a difference in chemical shift of 1.20 τ, which is in a direction opposite to that predicted from the electronegativity of oxygen and sulfur. This has been rationalized on the basis of the dominating influence of resonance placing a negative charge on carbon number 2 over the relative inductive effect of oxygen and sulfur.

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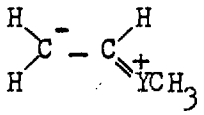
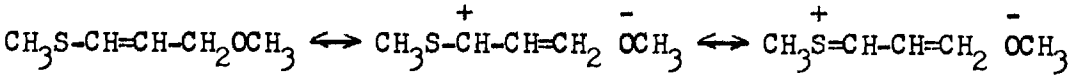
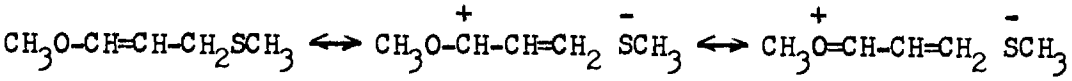
20. J. H. Goldstein, <u>J. Phys. Chem.</u>, <u>67</u>, 110 (1963).



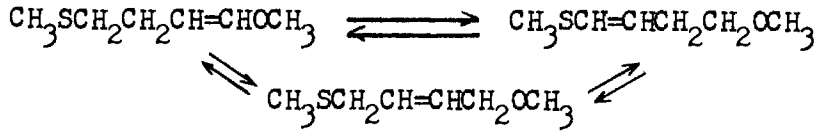
(Y = O, S)

A complication to interpretation of the results of reaction number 3 is due to possible stabilization of the two isomers by resonance involving structures bearing a formal negative charge on oxygen or sulfur. Clearly, such resonance would favor the vinyl ether and provide another





driving force that the electronegativity effect must overcome in order to dominate the equilibrium. This complication could be eliminated, at the probable expense of increasing the experimental difficulty, by studying the butene system.



(4

The ready availability of a large number of equilibrium data for

derivatives of unsaturated carbonyl compounds provide a convenient framework for the study of the relative ability of alkoxy and thioalkoxy groups to stabilize double bonds. A comparison of the equilibrium constants for 4-methoxy and 4-methylthio substituted methyl butenoates seem best suited for this purpose.

$$Y\text{-}CH_2CH{=}CHCO_2CH_3 \rightleftharpoons Y\text{-}CH{=}CHCH_2CO_2CH_3 \qquad (5$$
$$(Y = CH_3O,\ CH_3S)$$

The effect of alkoxy groups upon the stability of alkynes has never, to my knowledge, been demonstrated. A study of the equilibrium between 1-methoxypropyne and 2-methoxypropyne offers a possibility of demonstrating the electronegativity effect. The electronegativity effect

$$CH_3OCH_2C{\equiv}CH \rightleftharpoons CH_3OCH{=}C{=}CH_2 \rightleftharpoons CH_3OC{\equiv}CCH_3 \qquad (6$$

should be greater than in the alkenes since the carbon attached to oxygen is undergoing a change from $\underline{sp}^3$ to $\underline{sp}$ hybridization. Also there is reason to believe that the complicating resonance interactions between the triple bond and the unshared electron pairs on oxygen should be relatively small.

The fact that benzoic and crotonic acids are weaker than would be calculated from the Taft equation has been attributed to resonance stabilization of the acids due to conjugation between the corboxyl group and the aromatic ring or double bond; such resonance stabilization should

be much smaller in the carboxylate anion (21, 22). Since the acidity of phenylpropiolic acid deviates much less (but in the same direction) from the Taft-equation value, it appears that resonance interaction of the carboxyl group with a triple bond is much smaller than with a double bond or an aromatic ring (22). This may be due to the greater overlap of the pi orbitals on the carbon atoms of the triple bond, resulting from the shorter carbon-carbon bond length. If this is so, alkoxyacetylenes should be less stabilized by resonance than alkoxyolefins. There is evidence that the oxygen atom of an alkyne ether participates in resonance with the triple bond while the sulfur atom of an alkyne thioether does not. Drenth and Loewenstein (23) have observed in the n.m.r. spectra of a number of acetylenic ethers a large shift of the acetylenic proton to low field which they attribute to oxygen-electron-pair delocalization into the triple bond. A similar conclusion was reached by studying the dipole moments of acetylenic ethers (24). No evidence for such a charge shift in acetylenic thioethers was found.

Arens and co-workers (25) have observed that 1-butoxypropyne is converted to the sodium salt of 3-butoxypropyne by the action of one

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21. R. W. Taft, Jr. and D. J. Smith, J. Am. Chem. Soc., 76, 305 (1954).

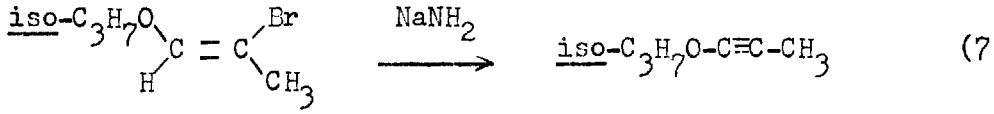
22. J. Hine and W. C. Bailey, Jr., J. Am. Chem. Soc., 81, 2075 (1959).

23. W. Drenth and A. Loewenstein, Rec. Trav. Chim., 81, 635 (1962).

24. W. Drenth, G. L. Hekkert, and B. G. Zwaneburg, Rec. Trav. Chim., 79, 1056 (1960); 81, 313 (1962).

25. J. J. van Daalen, A. Kraak, and J. F. Arens, Rec. Trav. Chim., 80, 810 (1961).

equivalent of sodium amide in liquid ammonia, but here the driving force is due to formation of the sodium salt of the terminal acetylene. The action of 0.95 equivalents of sodium amide on trans-2-bromo-1-iso-propoxypropene gives 1-iso-propoxypropyne with only trace amounts of the allene and the terminal acetylene (25) while trans-2-bromo-1-phenoxy-1-propyne gives only phenoxyallene on treatment with potassium hydroxide (26). Under the conditions of the elimination reaction, phenoxyallene



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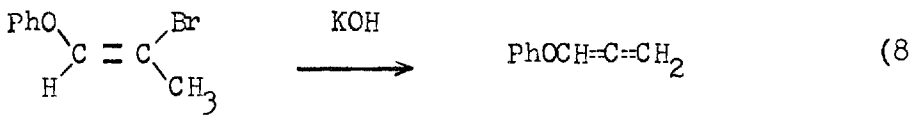

(8

and 1-phenoxy-1-propyne were not interconverted. Heating 1-alkoxypropyne with potassium hydroxide powder at 150° for 3.5 hours gives almost quantitative recovery with only trace amounts of alkoxy allene present as shown by the infrared spectrum (27). Apparently the presence of an alkoxy group renders these interconversions exceedingly difficult.

Such is not the case with the thioalkoxy propynes. The stability of the isomers of thioalkoxypropyne were found to be 1-thioalkoxypropyne

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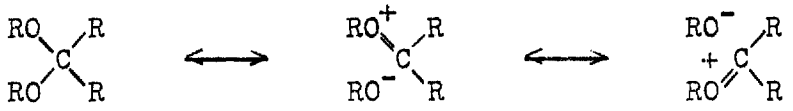
26. L. F. Hatch and H. D. Weiss, J. Am. Chem. Soc., 77, 1798 (1955).

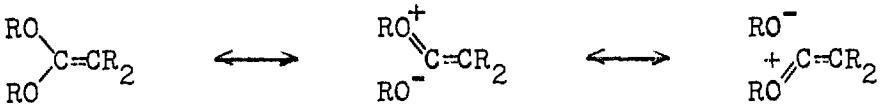
27. J. R. Nooi and J. F. Arens, Rec. Trav. Chim., 78, 284 (1959).

> thioalkoxyallene > 3-thioalkoxypropyne (28, 29). The activating influence of sulfur is such that these equilibrations can be achieved with sodium ethoxide in ethanol at 25 to 80°.

In view of the interest of this laboratory in double bond - no bond resonance, we decided to investigate the equilibrium between 3,3-dimethoxy-1-propene and 1,1-dimethoxy-1-propene. Compounds having two alkoxy groups attached to the same, saturated, carbon atom show an enhanced stability ($\approx$ 7 kcal/mole) which has been rationalized by Hine (30) in terms of non-bonded resonance structures. This double bond - no



bond resonance may be unimportant when the carbon atom bearing the alkoxy groups is unsaturated since the geometery of this system would be very unfavorable.



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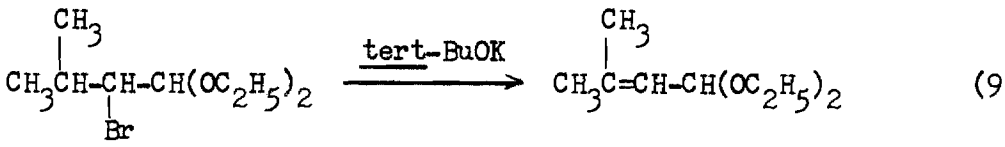
28. L. Brandsma, H. E. Wijers, and J. F. Arens, Rec. Trav. Chim., 82, 1040 (1963).

29. G. Pourcelot, P. Cadiot and A. Willemart, Compt. Rend., 252, 1630 (1961).

30. J. Hine, J. Am. Chem. Soc., 85, 3239 (1963).

McElvain, Clarke, and Jones (31) moted that the dehydrobromination of the diethylacetal of alpha-bromoisovaleraldehyde gives the acetal of an alpha-beta-unsaturated aldehyde rather than the ketene acetal (which was shown to be stable under the reaction conditions). This result could be explained in terms of double bond - no bond resonance due to the two



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oxygen atoms attached to the same saturated carbon atom in the reactant. However, it is not clear that the dehydrobromination product was the thermodynamically more stable isomer. Rothstein (32) has attempted the equilibration of 1,1-diethoxypropene and 3,3-diethoxypropene using potassium tert-butoxide in refluxing tert-butyl alcohol without success.

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31. S. M. McElvain, R. L. Clarke, and G. D. Jones, J. Am. Chem. Soc., 64, 1966 (1942).

32. E. Rothstein, J. Chem. Soc., 1558 (1940).

CHAPTER II

EXPERIMENTAL RESULTS

Chemicals[1]

Buffer Solution. A standard Beckman pH 7 buffer was used.

Dimethyl Sulfoxide. Baker dimethyl sulfoxide was dried by distilling from calcium hydride at reduced pressure on column number 2.[2] The distillate was passed through a 2.4 X 26 cm. column filled with Lindy 5A molecular sieves and lead directly to oven dried ampoules. These ampoules were then sealed under nitrogen. In all of these operations (except the distillation) the dimethyl sulfoxide was kept under a positive pressure of nitrogen.

3,3-Dimethoxypropene. Shell Development Corporation 3,3-dimethoxypropene was distilled on column number 1. This material was judged pure by analysis on g.l.c. instrument number 1 using a silicone grease column at 160°.

Dimsylsodium. Dimsylsodium, the sodium salt of dimethyl sulfoxide, was prepared by heating stock sodium hydride power and dimethyl sulfoxide at 55° until evolution of hydrogen almost ceased. The mixture was then filtered through a fritted glass filter. Positive nitrogen pressure was

[1] Elemental analyses were preformed by Galbraith Labortories, Inc., Knoxville, Tennessee.

[2] The columns are discussed in the section on equipment.

maintained throughout the procedure.

Methanol. Stock methanol was dried using magnesium metal (33).

Methyl Mercaptan. Matheson methyl mercaptan was used.

Nitrogen. Commercial prepurified nitrogen was used which is said by the supplier to be 99.999 per cent pure.

Potassium tert-Butoxide. The MSA Research Corportion product was used.

Sodium Methoxide. A Fisher Scientific Company product was used.

tert-Butyl Alcohol. Baker reagent grade tert-butyl alcohol was used.

Triethylamine. Eastman triethylamine was distilled from potassium hydroxide.

Synthesis of 1-Chloro-3-methoxy-2-propanol (II). This compound was prepared according to the procedure of Gallardo and Pollard (34) in 82 per cent yield, boiling 76 to 76.5° at 20 mm. The reported boiling point is 76.5° at 20 mm.

Synthesis of 2-Hydroxy-1-methoxy-3-methylthiopropane. A stream of methyl mercaptan was passed into a solution of 50 g. (2.17 mole) of sodium metal in one liter of methanol until the weight increase was 104 g. (2.17 mole). The flask was fitted with a reflux condenser and 280 g. (2.17 mole) of 1-chloro-2-hydroxy-3-methoxypropane was added. The solution was refluxed for 16 hours, concentrated, filtered and distilled at 20 mm. The product, 242 g., was collected at 100 to 102° in 82 per cent yield.

33. L. F. Fieser, "Experiments in Organic Chemistry," 3rd ed., D. C. Heath and Co., Boston, 1955, p. 289.

34. H. Flores Gallardo and C. B. Pollard, J. Org. Chem., 12, 831 (1947).

Anal. $C_5H_{12}O_2S$

calculated: C 44.09; H 8.88; S 23.54

found: C 44.02; H 8.96; S 23.70

The n.m.r. spectrum of the neat liquid shows a singlet at 6.02 τ, a broad multiplet centered about 6.2 τ, a doublet (J = 5 c.p.s.?) at about 6.85 τ which was partially masked by the following peak, a singlet at 6.67 τ, a doublet (J = 6 c.p.s.) at 7.43 τ, and a singlet at 7.89 τ. The relative areas were 1.1, 0.7, 2.3, 2.8, 1.9, and 3.0 respectively.

Synthesis of 2-Acetoxy-1-methoxy-2-methylthiopropane (IV). In a flask fitted with a drying tube and stirrer was placed 47.5 g. (0.60 mole) of distilled pyridine, 61.3 g. (0.60 mole) of acetic anhydride, and 64.5 g. (0.50 mole) of 2-hydroxy-1-methoxy-3-methylthiopropane. The mixture was cooled with an ice bath and allowed to stir overnight. Water was then added and the mixture was extracted with ether. The ether extract was washed with dilute hydrochloric acid and then water. The ether layer was then dried over Drierite, concentrated, and distilled at 3 mm. on column number 1. The product, 64.4 g., was collected at 92 to 93° in 74 per cent yield, $n^{27}D$ 1.4587. This material was judged pure by g.l.c. analysis on instrument number 1 using a 20 foot carbowax 20 M column at 160°.

Anal. $C_7H_{14}O_3S$

calculated: C 47.17, H 7.92, S 17.99

found: C 46.98, H 8.04, S 18.11

Synthesis of 3-Methoxy-1-methylthio-1-propene (V). Pyrolysis of 2-acetoxy-1-methoxy-3-methylthiopropane was carried out using a heated 2.2 cm. by 36 cm. tube containing glass helices and a high temperature

thermometer. The column was mounted vertically in a combustion furnance and was fitted at the top with a nitrogen inlet and a capillary-liquid-feed tube. A charge consisting of 54.3 g. of benzene and 27.2 g. (0.158 mole) of the acetate was passed through the column at 420 to 430° at a rate of three drops per minute with a nitrogen flow of 120 ml. per minute. A total of 76.9 g. of condensate was collected in a series of cold traps. This condensate was washed with sodium bicarbonate solution, then with water, and dried over Drierite. Careful distillation at 16 mm. on column number 1 gave fractions totaling 4.4 g. boiling from 59 to 67°. Analysis using g.l.c. instrument number 1 with a 20 foot carbowax 20 M column at 160° indicated cis-trans mixtures of 3-methoxy-1-methylthiopropene ranging from about 79 per cent cis and 21 per cent trans for the lower boiling fraction to 5 per cent cis and 95 per cent trans for the higher boiling fraction. Traces (about one per cent), of cis and trans isomers of 1-methoxy-3-methylthiopropene could be detected in these fractions using n.m.r. spectroscopy. The isomeric cis compounds have the same retention times on the g.l.c. column above as well as on a silicone grease, a PDEAS, and an Apiezon L column. The same was true for the isomeric trans compounds.

Anal. $C_5H_{10}OS$

calculated: C 50.81; H 8.53; S 27.13

(77 per cent cis, 23 per cent trans) found: C 50.61; H 8.67; S 27.09

(5 per cent cis, 95 per cent trans) found: C 50.68; H 8.58; S 27.25

The infrared spectra are given in Figures 1 and 2. The n.m.r. data is given in tabular form in Table 10.

Synthesis of 3-methoxy-1-methylthiopropene was also attempted by addition of methyl mercaptan to methyl propargyl ether. A mixture of 9.6 g. (0.20 mole) of methyl mercaptan, 14.2 g. (0.20 mole) of methyl propargyl ether, and 0.1 g. of benzoyl peroxide was sealed in a Carius tube and irradiated with a General Electric RS sun lamp for 64 hours. The tube was opened and its contents were distilled on column number 1. Some methyl propargyl ether was recovered but no methyl mercaptan. The pressure was reduced to 42 mm. giving a fraction (2.4 g.) boiling mainly at 134°. The n.m.r. spectrum of the latter was consistent with 1,2-dimethylthio-3-methoxypropane, which is reported (35) to boil 110 to 114° at 15 mm.

Redistillation at 101 mm. of the fraction boiling 73 to 122° gave fractions, totaling 0.9 g., which boiled from 94 to 105°. Analysis on g.l.c. instrument number 2 using Perkin-Elmer column O at 152° indicated various cis-trans mixtures of 3-methoxy-1-methylthiopropene of about 80 per cent purity. The n.m.r. spectra were consistent with this finding.

The initial reaction product, analyzed by g.l.c. as above, contained about nine times more 1,2-dimethylthio-3-methoxypropane than 3-methoxy-1-methylthiopropene. Small scale experiments were carried out using larger ratios of methyl propargyl ether to methyl mercaptan, with and without peroxide and ultraviolet irradiation, with little success in improving the product ratio.

Synthesis of 1,1,3-Trimethoxypropane (VII). This compound was prepared by a procedure similar to that for the synthesis of 1,1,3-

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35. P. S. Fitt and L. N. Owen, J. Chem. Soc., 2250 (1957).

triethoxypropane (36). In a three necked flask fitted with a reflux condenser, drying tube, and stirrer was placed 210 ml. (3.1 mole) of acrolein, 385 ml. of dry methanol, and 11 g. of ammonium chloride. The mixture was stirred for one hour at room temperature and then the temperature was slowly raised to 68° over a three hour period. After stirring for an additional hour at 68° the flask was cooled, 120 g. of anhydrous sodium sulfate was added, and the mixture allowed to stand for two days. The mixture was filtered, distilled to free of acrolein, and then redistilled on column number 2 at 133 mm. pressure. A fraction boiling 50 to 52.5° was collected (27.4 g.) which was 3-methoxypropionaldehyde in 10 per cent yield. The reported boiling point is 50° at 125 mm. (37). The second fraction, 6.9 g., boiling 52.5 to 59° was a mixture of 3-methoxypropionaldehyde and 1,1,3-trimethoxypropane. The third fraction (35.4 g.) boiling 79 to 84° was 1,1,3-trimethoxypropane in 9.3 per cent yield. The reported boiling range is 94 to 95° at 142 mm. (38).

Synthesis of 1,1-Dimethylthio-3-methoxypropane (VIII). A mixture of 30.9 g. (0.35 mole) of 3-methoxypropionaldehyde, 38.9 g. (0.29 mole) of 1,1,3 - trimethoxypropane, 80 ml. (1.41 mole) of methyl mercaptan, and 0.9 ml. of 13.5 M methanolic hydrogen chloride was sealed in Carius tubes. After 24 hours at room temperature the tubes were opened and purged with nitrogen to remove excess methyl mercaptan. The solution was made

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36. E. C. Horning (ed.-in-chief), "Organic Syntheses," collective Volume III, John Wiley and Sons, New York, 1955, p. 371.

37. K. F. Beal and C. J. Thor, J. Polym. Sci., 1, 543 (1946).

38. R. H. Hall and E. S. Stern, J. Chem. Soc., 2657 (1955).

slightly basic by adding sodium hydroxide. The mixture was extracted with ether, and the extract was dried over magnesium sulfate. Distillation at 42 mm. pressure through a 13 cm. glass helix packed column gave 42.0 g. of product boiling 124.5 to 129° in 40 per cent yield. This material was judged pure by analysis on g.l.c. instrument number 2 using column 0 at 130°.

Anal. $C_6H_{14}OS_2$

calculated: C 43.33; H 8.49; S 38.56

found: C 43.51; H 8.27; S 38.67

The n.m.r. spectrum of the neat liquid shows a triplet (J = 7.5 c.p.s.) at 6.17 τ, a triplet (J = 6.2 c.p.s.) at 6.51 τ, a singlet at 6.72 τ, a singlet at 7.95 τ, and a triplet split further into doublets (J = 6.2 and 7.5 c.p.s.) at 8.08 τ. The relative areas were 1.03, 1.98, 2.98, 5.96, and 2.05 respectively.

Attempted Synthesis of 3-Methoxy-1-methylthio-1-propene (V). The elimination of methyl mercaptan from 1,1-dimethylthio-3-methoxypropane to produce 3-methoxy-1-methylthiopropene was attempted in several ways.

Acid catalyzed elimination of methyl mercaptan was attempted by a method similar to that of Sprozynski (39). A mixture of 0.2 ml. of 1,1-dimethylthio-3-methoxypropane and 0.003 ml. of 86 per cent phosphoric acid was heated over the range of 110 to 190° over several hours without evolving methyl mercaptan as measured by a gas burette. The material formed a dark viscous mass as a result of the heating.

In a second attempt, a flask was washed with 1 M sulfuric acid,

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39. A. Sporzynski, Chem. Zentr., II, 1704 (1936).

dried, and charged with 13.8 g. of 1,1-dimethylthio-3-methoxypropane and 20 ml. of distilled diphenyl ether. The flask was attached to a fractionation assembly having a 30 cm. glass helix packed column and was heated to 245° for 17 hours. The material was then distilled at reduced pressure until the diphenyl ether began to come over. This distillate was then processed on g.l.c. instrument number 1 using a silicone grease column with a 100 to 155° program. The fractogram showed only one major product; it had a retention time less than that of the starting material and its area was about 0.53 of that of the starting material. Preparative seale g.l.c. gave 0.5 g. of this material. The n.m.r. spectrum showed a complex structure centered at 4.4 τ, a doublet (J = 7 c.p.s.) at 6.9 τ, a singlet at 7.8 τ, and a singlet at 8.0 τ. The relative areas were 1.9, 1.9, 3.0, and 3.1 respectively.

Vapor phase pyrolysis as employed by Hall (38) for elimination of methanol from acetals were carried out in a column packed with glass helicies. Nitrogen was employed as a carrier gas using a volume ratio of 1,1-dimethylthio-3-methoxypropane to nitrogen of 1:2 and a contact time of about 1.5 minutes. The temperature was varied from about 370 to 410° without observing any 3-methoxy-1-methylthiopropene as judged by n.m.r. analysis. At the higher temperatures the n.m.r. spectrum of the condensate showed bands at 3.0 τ indicative of aromatic protons. A similar procedure using aluminia and glass helices as column packing at temperatures of 300 to 350° gave no product.

Synthesis of 3-Methylthiopropionaldehyde (XII). Synthesis of 3-

methylthiopropionaldehyde was accomplished by the method of Heilbron (40) and co-workers except acrolein was added to a mixture of triethylamine and methyl mercaptan in order to minimize polymerization of acrolein. The product was obtained in 62 per cent yield, boiling 95 to 96° at 60 mm. The refractive index was $n^{25}D$ 1.4803. The reported values are boiling point 166° at 750 mm. and $n^{20}D$ 1.4824. This material was judged pure by analysis on g.l.c. instrument number 1 using a silicone grease column at 160°.

Synthesis of 1-Methoxy-3-methylthio-1-propene (XIV). This two-step synthesis was accomplished by a general procedure (41) for the preparation of vinyl ethers.

A mixture of 61.7 g. (0.59 mole) of 3-methylthiopropionaldehyde and 100 ml. of n-hexane was placed in a three-necked flask fitted with ice condensed, stirrer, addition funnel, and gas addition tube. The flask was placed in an ice bath and dry hydrogen chloride gas was passed in while 18.9 g. (0.59 mole) of dry methanol was added slowly. The mixture was saturated with hydrogen chloride gas for 20 minutes after addition of methanol was complete. The upper layer was then decanted, 80 g. (0.66 mole) of N,N-dimethyl aniline was added to the upper layer, and the mixture was heated to reflux for one hour. Two layers were produced. The dark lower layer was separated from the hexane layer and extracted with ether after adding a small amount of water. The hexane layer and the ether extract were combined, dried over Drierite, and

40. J. R. Catch, A. H. Cook, A. R. Graham, and Sir Ian Heibron, J. Chem. Soc., 1609 (1947).

41. H. R. Warner and W. E. M. Lands, J. Am. Chem. Soc., 85, 60 (1963).

concentrated. Distillation of this material on column number 1 at 17 mm. gave 20.2 g. of cis and trans product in 29 per cent yield. The boiling range at 17 mm. was 59 to 67°.

The mixture of cis and trans isomers was carefully distilled on column number 1 at 17 mm. pressure and seven fractions were collected over a temperature range of 56 to 64°. The fractions were analyzed using g.l.c. instrument number 1 and PDEAS column at 160°. The cis and trans isomers had retention times of 4.5 and 5.5 minutes respectively. Using the product of peak height and retention time as a measure of the relative amounts present, the initial fraction, boiling 56 to 58°, contained about 73 per cent of the cis isomer and 27 per cent of the trans isomer. The last fraction, boiling 63.5 to 64°, $n^{25}D$ 1.4898, contained about 9 per cent cis isomer and 91 per cent trans isomer. Analysis by n.m.r. spectroscopy confirmed these figures.

A separation of the cis isomer was carried out using the g.l.c. instrument as above. There was obtanied about 0.2 ml. of material which contained less than 11 per cent of the trans isomer. The infrared spectra of the predominate cis and trans mixtures are reproduced in Figures 3 and 4. The n.m.r. data is given in tabular form in Table 9.

Anal. $C_5H_{10}OS$

	calculated:	C 50.81; H 8.53; S 27.13
(9 per cent cis, 91 per cent trans)	found:	C 50.70; H 8.41; S 26.95
(89 per cent cis, 11 per cent trans)	found:	C 50.78; H 8.42; S 26.98

Synthesis of 3-Chloropropionaldehyde Dimethylacetal (XV). The synthesis of 3-chloropropionaldehyde dimethylacetal was accomplished by

the procedure of Wohl and Momber (42). The product $n^{29}D$ 1.4186, boiled 88.5 to 89.0° at 100 mm. The reported boiling range is 80 to 89° at 100 mm.

The n.m.r. spectrum of the neat liquid shows a triplet at 5.48 τ (J = 5.5 c.p.s.) due to the acetal carbon proton, a triplet at 6.44 τ (J = 6.9 c.p.s.) due to the carbon three protons, a singlet at 6.70 τ due to the methoxy protons, and a triplet split further into a doublet at 8.00 τ (J = 6.9 and 5.5 c.p.s.) due to the methylene protons. The relative areas were 1.1, 2.2, 5.9, and 2.1 respectively.

Synthesis of 3-Methylthiopropionaldehyde Dimethylacetal (XVI). Liquid methyl mercaptan, 26 ml. (0.49 mole), was carried in a nitrogen stream to a solution of 12.0 g. (0.52 mole) of sodium metal in 220 ml. of absolute ethanol. The resulting solution of sodium thiomethoxide was heated under reflux while adding 67.0 g. (0.48 mole) of 3-chloropropionaldehyde dimethyl acetal slowly with stirring. The excess alcohol was removed on a steam bath and the concentrate was filtered free of sodium chloride. The salt was washed with three 15 ml. portions of 95 per cent ethanol; the filtrate and washing were combined, concentrated, and distilled on column number 2 at 44 mm. pressure. The 3-thiomethylpropionaldehyde dimethylacetal was collected at 102 to 103° (51.7 g.) in 72 per cent yield. The refractive index is $n^{29}D$ 1.4516. This material was judged pure by analysis on g.l.c. instrument number 3 using a column temperature of 172°.

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42. A. Wohl and F. Momber, Ber., 47, 3346 (1914).

Anal. $C_6H_{14}O_2S$

calculated: C 47.97; H 9.39; S 21.34

found: C 47.77; H 9.19; S 21.14

The n.m.r. spectrum of the neat liquid shows a triplet at 5.55 τ (J = 5.6 c.p.s.) due to the proton of the acetal carbon, a singlet at 6.73 τ due to the methoxy protons, a multiplet at 7.52 τ due to the 3-carbon protons, a singlet at 7.96 τ due to the methylthio protons, and a multiplet at 8.21 τ due to the methylene protons. The respective areas are 1.04, 5.90, 2.02, 3.02, and 2.02.

Attempted synthesis of 1-Methoxy-3-methylthiopropene (XIV). According to the procedure of Voronkov (43) for the preparation of vinyl ethers, a distillation apparatus with a 30 cm. glass helix packed column was charged with 39 g. of 3-methylthiopropionaldehyde dimethyl acetal; and the pot temperature was held at 170° for 80 minutes while distilling methanol as it was formed. The pot residue was then distilled at 13 mm. pressure giving an impure fraction (6.36 g.) boiling at 57°, which contained 1-methoxy-3-methylthiopropene as judged by its n.m.r. spectrum. It was not possible to get pure material from this fraction by redistillation. The use of a trace of p-toluenesulfonic acid as catalyst gave equally poor results.

Synthesis of trans-1-Methoxy-4-methylthio-2-butene (XIX). In a three-necked flask fitted with dropping funnel, condenser, and stirrer was placed 126 g. (1.00 mole) of freshly distilled Eastman trans-1,4-dichloro-2-butene and 100 ml. of dry methanol. Over a period of 30 minutes 333 ml.

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43. M. G. Voronkov, J. Gen. Chem. USSR, 20, 2131 (1950).

of 3.0 M sodium methoxide in methanol was added through the dropping funnel with stirring. The heat evolved was sufficient to bring the solution to the reflux temperature. After standing for one hour the solution was found to be 0.01 M in base.

A solution of 40 g. (1.00 mole) of sodium hydroxide in 200 ml. of methanol was saturated with methyl mercaptan and then added to the reaction mixture. The mixture was stirred overnight and filtered. The salt was washed with two 100 ml. portions of methanol and the methanol solutions were combined and concentrated. Water was added to the concentrate and all extracted with hexane. The hexane extract was washed with water, separated, and dried over Drierite. Distillation was carried out on column number 2, after concentration, at a pressure of 48 mm. The product (33 g.) was collected at 101.5 to 103° in 25 per cent yield. A fore-run of 20 g. of trans-1,4-dimethoxy-2-butene was collected at 68 to 75°. The reported (44) boiling point is 50° at 20 mm. for a product of undefined stereochemistry.

The original reaction mixture was examined on g.l.c. instrument number 3 using Golay column Q at 150° and 30 p.s.i. helium pressure. Only three products were found: 1) trans-1,4-dimethoxy-2-butene (R_t = 2.1 min.); 2) trans-1-methoxy-4-methylthio-2-butene (R_t = 6.3 min.); 3) probable trans-1,4-bis(methylthio)-2-butene (R_t = 17.6 min.) .

Distillation of the 101.5 to 103° fraction (above) on column number 1 at 30 mm. gave pure trans-1-methoxy-4-methylthio-2-butene boiling at 91°, $n^{25}D$ 1.4839. The infrared spectrum is given in Figure 5 and the n.m.r.

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44. A. A. Petrow, Zh. Obshch, Khim., 19, 1046 (1949).

spectrum is given in Figure 10.

Anal. $C_6H_{12}OS$

calculated: C 54.50; H 9.15; S 24.25

found: C 54.63; H 9.07; S 24.46

Synthesis of Methyl Crotonate. Methyl crotonate was prepared according to the procedure of Vogel (45). The product boiled 118 to 120°; the reported value is 118 to 120°.

Synthesis of Methyl 4-Bromocrotonate (XXIV). Methyl 4-bromocrotonate was prepared according to the procedure of Schmid and Karrer (46) in 52 per cent yield. The product boiled 85 to 87°. The reported boiling range is 87 to 91° at 13 mm. This material is very painful on the skin.

Synthesis of Methyl 4-methoxycrotonate (XXV). Methyl 4-methoxycrotonate was prepared according to the procedure of Sultanbawa and Veeravagu (47). The product boiled 73 to 75° at 12 mm. The reported boiling range is 76 to 78° at 12 mm. The n.m.r. spectrum is reported in tabular form in Table 7. This material was judged pure by analysis on g.l.c. instrument number 1 using PDEAS column at 170°.

Synthesis of Methyl cis-4-Methoxy-3-butenoate (XXVI). To a mixture of 11 ml. of dry tert-butyl alcohol (Baker reagent grade) and 0.5 ml. of 2 M sodium methoxide in methanol was added 1.80 g. (0.0138 mole) of methyl 4-methoxycrotonate. The solution was heated at 45° for 15 minutes and

45. A. I. Vogel, "A Text-book of Practical Organic Chemistry," 3rd ed., Longmans, Green and Co., London, 1956, p. 927.

46. H. Schmid and P. Karrer, Hel. Chim. Acta, 29, 573 (1946).

47. M. Sultanbawa and P. Veeravagu, J. Chem. Soc., 1262 (1960).

then was quenched with pH 7 buffer solution (Beckman) which contained sufficient acetic acid to neutralize the sodium methoxide. The mixture was extracted with chloroform; the extract was washed with water to remove the tert-butyl alcohol. The chloroform extract was dried over magnesium sulfate and concentrated under 30 mm. pressure to give 1.3 g. of crude methyl cis-4-methoxy-3-butenoate. Analysis on g.l.c. instrument number 1 using a PDEAS column at 180° gave three overlapping peaks followed by a resolved peak. The first was a large peak due to the methyl cis-4-methoxy-3-butenoate. The second peak was very small and is probable due to methyl trans-4-methoxy-3-butenoate. The third peak was also very small and had the retention time of the starting material. The fourth peak was about 0.1 the size of the first peak and it had the retention time of methyl 3,4-dimethoxybutanoate which has been observed in the study of the addition of methanol to methyl 4-methoxycrotonate.

Distillation of the crude product on column number 1 gave material boiling 74 to 76° at 15 mm. A pure sample of methyl cis-4-methoxy-3-butenoate was obtained by preparative g.l.c. (as above), $n^{25}D$ 1.4348. The n.m.r. data is given in tabular form in Table 7 and the infrared spectra is given in Figure 6.

Anal. $C_6H_{10}O_3$

calculated: C 55.37; H 7.75

found: C 55.28; H 7.72

Synthesis of Methyl 4-Methylthiocrotonate (XXVII). The procedure used for the preparation of methyl 4-methylthiocrotonate was that of Birkofer and Hartwig (48). A rapid distillation on column number 1 at

48. L. Birkofer and I. Hartwig, Chem. Ber., 87, 1189 (1954).

approximately 1 mm. pressure[1] gave reasonably pure product, uncontaminated with its isomers (by n.m.r. spectroscopy), boiling about 50°. The yield was 72 per cent. The reported boiling range is 89 to 99°[2]. Redistillation of the material above gives pure material, boiling 99.0°, $n^{25}D$ 1.4995. This material was judged pure by analysis on g.l.c. instrument number 3 at 175°. The n.m.r. spectrum is given in tabular form in Table 8. The infrared spectrum is given in Figure 7.

Synthesis of cis and trans Methyl 4-Methylthio-3-butenoate (XXIX) and (XXVIII). A 15 ml. sample of methyl 4-methylthiocrotonate was heated with 2.0 ml. of triethyl amine overnight at 100° and was then distilled at 12 mm. on column number 1. A mixture of methyl 4-methylthiocrotonate and the methyl esters of cis and trans-4-methylthio-3-butenoate (14 ml.) distilled over the range of 88 to 99°. The higher boiling fractions were mostly methyl 4-methylthio-3-butenoate. Separation of these isomers was carried out on g.l.c. instrument number 1 with a PDEAS column at 190°. The observed retention times were methyl 4-methylthiocrotonate 13.8 min., methyl trans-4-methylthio-3-butenoate 12.7 min., and methyl cis-4-methylthio-3-butenoate 10.9 min. Small amounts of each beta-gamma isomer (ca. 0.4 g.) was obtained in reasonable pure form as judged by n.m.r. spectroscopy and g.l.c. analysis. The sample of the cis isomer contained ca. 3 per cent of the trans isomer and ca. 2 per cent of the crotonate.

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[1] Distillation at 12 mm., the procedure of Birkofer and Hartwig (48), gives a partially isomerized product. This probably is due to traces of amine salt which isomerize the compound.

[2] Compare this with the boiling range of the isomeric mixture (this page).

The sample of the trans isomer contained ca. 3 per cent of the cis isomer and ca. 7 per cent of the crotonate.

Anal. $C_6H_{10}O_2S$

	calculated:	C 49.28; H 6.89; S 21.93
(cis isomer)	found:	C 49.10; H 7.00; S 21.91
(trans isomer)	found:	C 49.16; H 6.95; S 21.95

The n.m.r. data are given in tabular form in Table 8 and the infrared spectra are given in Figures 8 and 9.

Synthesis of Methyl Propargyl Ether (XXI). In a three-necked flask fitted with stirrer and dropping funnel was placed 112.2 g. (2.00 mole) of propargyl alcohol (General Aniline), 80 g. (2.00 mole) of sodium hydroxide, and 200 ml. of water. The flask was cooled at 13° in an ice bath and 20 ml. of the 268 g. (2.10 mole) of dimethyl sulfate was added with stirring. After ten minutes the rest of the dimethyl sulfate was added over 30 minutes while keeping the temperature between 15 and 20°. The mixture was then stirred for 30 minutes in the ice bath; the upper layer was separated, dried over magnesium sulfate, and distilled from a Claisen flask. The methyl propargyl ether, 86.6 g., was collected from 61 to 62° in a 62 per cent yield. The reported boiling range is 63 to 64° (49). This material was judged pure by analysis on g.l.c. instrument number 2 using column A at 65°.

Synthesis of Methoxyallene (XXII). One hundred milliliters of dimethyl sulfoxide (Baker reagent grade) and 17 ml. of 3 M sodium methoxide in methanol was placed in a flask and the methanol removed under

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49. I. M. Heilbron, E. R. H. Jones, and R. N. Lacey, J. Chem. Soc., 27 (1946).

reduced pressure. The flask was heated to 90° and 10 ml. of methyl propargyl ether was introduced. After 15 minutes the product was removed under reduced pressure and collected in a dry ice trap. This process was repeated until a total of 40 g. (0.57 mole) of methyl propargyl ether had been processed. The condensate was extracted with three 10 ml. portions of concentrated potassium hydroxide solution to remove methanol. The material was then dried over potassium hydroxide. The material was distilled on column number 2 under nitrogen giving about 13 g. of methoxyallene boiling 50.8 to 52.2°, $n^{25}D$ 1.4244. This material was judged pure by analysis on g.l.c. instrument number 2 using column A at 65°. The low yield is chiefly due to evaporation losses and oxygen induced polymerization. During the distillation, accidental introduction of a small amount of air into the variable take off head caused the entire column to become plugged with polymer.

Anal. C_4H_6O

calculated: C 68.54; H 8.63

found: C 68.73; H 8.80

The n.m.r. spectrum of the neat compound shows a triplet (J = 6.0 c.p.s.) at 3.23 τ, a doublet (J = 6.0 c.p.s.) at 4.54 τ, and a singlet at 6.61 τ. The relative areas are 1.0, 2.0, and 3.0.

Synthesis of 1-Methoxypropyne (XXIII). The synthesis of 1-methoxypropyne was accomplished by the procedure of Alkema and Arens (50) for the synthesis of 1-ethoxypropyne. An insulated three-necked flask was fitted with stirrer, addition funnel, and dry ice condenser. The exit

50. H. J. Alkema and J. F. Arens, Rec. Trav. Chim., 79, 1257 (1960).

tube of the condenser was lead to a vapor scrubber containing diethyl ether and then to an ammonia scrub tower which emptied into the drain. The apparatus was provided with a means of by-passing the ether scrubber.

A stirred suspension of sodium amide in liquid ammonia was prepared from 17.9 g. (0.78 mole) of sodium metal and 600 ml. of anhydrous ammonia by the standard procedure. To this was added dropwise, 30.5 g. (0.246 mole) of chloroacetaldehyde dimethyl acetal (Eastman). No color change could be seen during this addition. The suspension was stirred for three hours and then 72 g. (0.505 mole) of methyl iodide (Fisher) was added over 30 minutes. During the addition the ether scrubber was connected and cooled to about -18° in an ice-salt bath. The dry ice condenser was allowed to warm up and let the exit gas pass through the ether scrubber. After stirring for 23 hours 125 ml. of ether was added to the reaction mixture and the remaining 350 ml. of liquid ammonia was allowed to evaporate by removing the insulation. During the reaction it was necessary to add a total of about one liter of ether to the scrubber in order to offset the evaporation losses. When the ammonia had completely evaporated, 150 ml. of water was added to the reaction flask and the mixture extracted with ether. The ammonia in the ether scrubber was allowed to escape by removing the ice-salt bath and this was then combined with the other ether solution. The combined solutions were dried over Drierite and distilled through a 30 cm., glass helix packed column. A fraction was obtained boiling 61 to 73° which weighed 4.10 g. The n. m.r. spectrum showed the presence of ethanol (an impurity in the diethyl ether) so this fraction was washed with two 2.0 ml. portions of water.

After drying over Drierite, the resulting product was judged to be about 90 per cent pure by g.l.c. and n.m.r. analysis. The reported boiling range is 65.7 to 66.3° (51).

The n.m.r. spectrum of the neat compound shows a singlet at 4.33 τ and a singlet at 8.50 τ. The relative areas are 1.00 and 0.99.

It appears that the difficulty in this preparation lies in the separation of the product from the relatively large amount of liquid ammonia.

Synthesis of Trimethyl Orthopropionate (XXXI). Trimethyl orthopropionate was prepared according to the procedure of Brooker and White (52). The product was obtained, boiling 121 to 124°, in 64 per cent yield. The reported boiling range is 126 to 128°.

Synthesis of Trimethyl 2-Bromoörthopropionate (XXXII). The preparation is similar to the method of Beyerstedt and McElvain (53) for the preparation of triethyl 2-bromoörthopropionate. In fact, the synthesis of 1,1-dimethoxypropene by this synthetic route will be reported soon (54).

To a stirred mixture of 53.5 (0.40 mole of trimethyl orthopropionate, and 31.6 g. (0.40 mole) of pyridine was added dropwise 64 g. (0.40 mole) of bromine over 30 minutes at 10°. The mixture was stirred three hours at 10° and then extracted with ether. The extract was con-

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51. J. R. Nooi and J. F. Arens, Rec. Trav. Chim., 78, 284 (1959).

52. L. G. S. Brooker and F. L. White, J. Am. Chem. Soc., 57, 2480 (1935).

53. F. Beyerstedt and S. M. McElvain, ibid., 59, 1273 (1937).

54. S. M. McElvain and J. T. Venerable, ibid., 72, 1661 (1959).

centrated and distilled at 60 mm. pressure in a Clasein flask. There was collected 39 g. of product boiling 85 to 100°. This was redistilled on column number 1 at 39 mm. pressure, giving 22.2 g. of product boiling 87 to 88° in 26 per cent yield.

Synthesis of 1,1-Dimethoxy-1-propene (XXXIII). The method used is according to the procedure of McElvain for the preparation of diethyl ketene acetal (55). In a three-necked flask fitted with stirrer, reflux condenser, drying tube, and dropping funnel was placed 150 ml. of p-xylene (dried over sodium), and 8.1 g. (0.355 mole) of sodium metal. This was heated, stirred, and cooled to from a sodium dispersion. The temperature was raised to 80° and 22.2 g. (0.104 mole) of trimethyl 2-bromoörtho-propionate was added over 40 minutes. The mixture was filtered to remove the blue salts and distilled on column number 1 until 20 ml. of distillate was collected. This was redistilled under nitrogen giving 5.6 g. of product boiling 99 to 100° in 53 per cent yield. The reported boiling range is 98 to 102°(54). This material polymerizes on storage for several months at -20°.

Instrumentation

Most of the equipment used for the experiments in this study have been described in part 1 of this thesis. Mention is only made here of additional equipment used, or of different operating procedures employed.

Constant-Temperature Bath. A Sargent constant-temperature water bath was used. The temperature was adjusted to within 0.2° using the National Bureau of Standards certified thermometer. No variation in

55. P. M. Walters and S. M. McElvain, J. Am. Chem. Soc., 62, 1482 (1940).

the temperature of the bath was observed using a thermometer graduated in tenths of a degree.

Infrared Spectrometer. A Perkin-Elmer Infrared Spectrum Model-237-B and a Model-337 was used. The instruments were operated as described in the operating manual. Reference spectra were recorded using a liquid film between sodium chloride discs. Frequency calibrations were made using a standard polystyrene film supplied by the manufacturer. The two instruments differ only in the wave length range covered. All measurements were made at a slit width setting of 6 and a fast scan speed.

Nuclear Magnetic Resonance Measurements. Quantitative measurements were made on a Varian Nuclear Magnetic Resonance Spectrometer, Model A-60. Various sweep rates were used in this study; however, care was taken to maintain the r.f. field control at the lowest possible setting (0.02 to 0.10 units) which gave a good signal to noise ratio without observing saturation effects.

Equilibration of 3-Methoxy-1-methylthiopropene

Isomerization of *cis* and *trans* 3-methoxy-1-methylthiopropene to *cis* and *trans* 1-methoxy-3-methylthiopropene is effected in dimethyl sulfoxide using potassium *tert*-butoxide as catalyst. The progress of the reaction is conveniently followed *in situ* by n.m.r. spectroscopy. The methoxy singlets of *cis* and *trans* 1-methoxy-3-methylthiopropene and the methylthio singlets of *cis* and *trans* 3-methoxy-1-methylthiopropene are well resolved, and the integrated areas under each singlet can be used to measure the relative concentration of each isomer.

A dimethyl sulfoxide solution was prepared containing 0.18 M

potassium tert-butoxide and 0.74 M cis and trans 3-methoxy-1-methylthiopropene. The solution was placed in a thin walled n.m.r. tube and heated at 50.0° unitl no further change was noted in the n.m.r. spectrum of the solution. An isomeric mixture was produced containing approximately 2 per cent trans and approximately 1 per cent cis vinyl sulfide. The trans-cis ratio of the vinyl ether produced was 2.06:1. This trans-cis ratio was shown to be the equilibrium value by equilibrating samples of the vinyl ether having trans-cis ratios of 5.0:1 and 0.67:1. The equilibration was carried out as before, and again the same final mixture was obtained. The measured trans-cis ratios of the vinyl ether were 2.07:1 and 2.08:1. The final values observed for the cis and trans vinyl sulfides were not shown to be the true equilibrium values; but their constancy, under conditions which still mobilize the slower cis-trans equilibration of the vinyl ether, suggests they must be very nearly so. The results of these equilibrations are presented in Table 2.

Attempted Equilibration of trans-1-Methoxy-4-methylthio-2-butene

Isomerization of trans-1-methoxy-4-methylthio-2-butene with base offers the possibility of involving no less than six isomeric compounds.

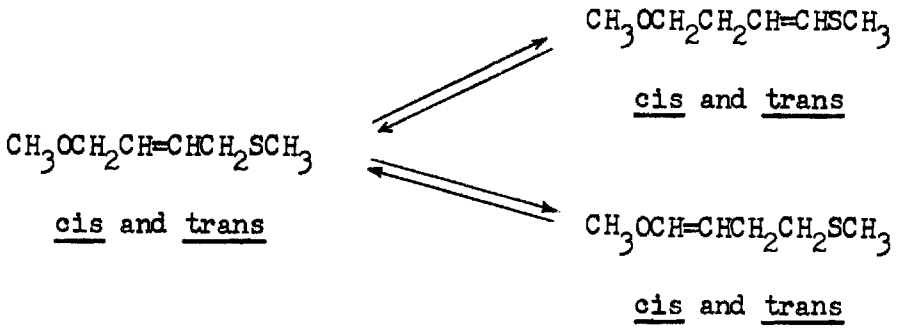

Table 2. Equilibration of the 1-Methoxy-3-methylthiopropenes at 50.0° in Dimethyl Sulfoxide[a]

0.18 M Potassium tert-Butoxide 0.74 M Total Olefin

Time (Minutes)	trans/cis Ratio of $CH_3OCH{=}CHCH_2SCH_3$	Number of Integrations[b]
Run 1[c]		
240	ca. 2.0	1
530	2.06 ± 0.08	4
Run 2[d]		
0	0.67	1
45	1.67	1
300	1.95 ± 0.15	4
480	1.99 ± 0.01	2
1200	2.07 ± 0.03	4
Run 3[d]		
0	4.96	1
45	2.28	1
300	2.00 ± 0.09	4
480	2.05 ± 0.01	2
1200	2.08 ± 0.08	4

[a] Estimated final mole per cent of 3-methoxy-1-methylthiopropene is ca. 2 per cent trans and ca. 1 per cent cis.

[b] Integration performed with a plaimeter.

[c] Initial sample was ca. 30 per cent cis and ca. 70 per cent trans 3-methoxy-1-methylthiopropene.

[d] Initial sample contained less than 10 per cent 3-methoxy-1-methylthiopropene.

If trans-1-methoxy-4-methylthio-2-butene is less stable than either 1-methoxy-4-methylthio-1-butene or 4-methoxy-1-methylthio-1-butene, the situation would be more hopeful. Hydrogen alpha to a sulfur atom is much more acidic than hydrogen alpha to an oxygen atom, and this might allow an equilibrium to be established between trans-1-methoxy-4-methylthio-2-butene and the vinyl sulfide before forming detectible amounts of the vinyl ether. Equilibrium between the vinyl ether and the vinyl sulfide could then be observed at longer reaction times.

This possibility was investigated by preparing a dimethyl sulfoxide solution 0.20 M in sodium methoxide and 0.10 M in trans-1-methoxy-4-methylthio-2-butene. The mixture was analyzed by diluting an aliquot of the solution with water, extracting this with n-pentane, and analyzing the extract by g.l.c. The g.l.c. instrument number 2 was used with a Perkin-Elmer diisodecyl phthalate column at 150°. The results of the experiment are given in Table 3. The data show that the ultimate products of the reaction are not isomers of the starting material, since their retention times (4.6 and 4.7 min.) are much shorter than that of the

Table 3. Analysis of the Isomerization of trans-1-Methoxy-4-methylthio-2-butene in Dimethyl Sulfoxide

0.20 M Sodium Methoxide 0.10 M Olefin

Sample History	Peak Height (inches) at Retention Times (mins.)			
	4.6	4.7	13.0	14.3
Start	0	0	0	ca. 95
One day at ca. 25°	26	20	27	60
5 minutes at 100°	40	31	19	29
15 minutes at 100°	74	64	5	9
60 minutes at 100°	89	97	2.5	4.1

starting material (14.3 min.). The two products were isolated by distillation from a small Claisen flask; the mixture came over between 61 and 65° at 48 mm. pressure. The n.m.r. spectrum in carbon tetrachloride contained two singlets of unequal height, at 7.90 and 7.92 τ as well as two complex bands centered about 6.4 and 5.4 τ. The infrared spectrum contained a strong absorption at 1600 cm^{-1}, which is characteristic of a conjugated diene. These data is consistent with a cis-trans mixture of 1-methylthio-1,3-butadiene, which could be formed by elimination of methoxide ion from the carbanion derived from 1-methoxy-4-methylthio-2-butene.

This reaction is similar to that found for the reaction between

$$CH_3O^- + CH_3OCH_2CH{=}CHCH_2SCH_3 \rightleftharpoons CH_3OH + CH_3OCH_2CH{=}C\dot{H}CHSCH_3$$

$$CH_3OCH_2CH{=}C\dot{H}CHSCH_3 \rightleftharpoons CH_3O^- + CH_2{=}CHCH{=}CHSCH_3$$

sodium amide and 1-alkoxy-2-butynes (56). The carbanion eliminated

$$ROCH_2C{\equiv}CCH_3 + NH_2^- \rightleftharpoons ROCH_2C{\equiv}CCH_2^- + NH_3$$

$$ROCH_2C{\equiv}CCH_2^- \longrightarrow RO^- + CH_2{=}C{=}C{=}CH_2$$

$$NH_2^- + CH_2{=}C{=}C{=}CH_2 \longrightarrow NH_3 + CH_2{=}CHC{\equiv}C^-$$

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56. L. Brandsma, P. P. Montijn, and J. F. Arens, Rec. Trav. Chim., 82, 1115 (1963).

alkoxide ion to produce a cumulene, which reacted further to produce the sodium salt of butenyne.

In view of this complication, no further attempts to equilibrate the 1-methoxy-4-methylthiobutenes were made.

Equilibration of the Methyl 4-Methylthiobutenoates

Base catalyzed isomerization of the methyl 4-methylthiobutenoates produces a total of four isomeric compounds. Methyl cis-4-methylthio-2-butenoate is not expected to contribute significantly to the equilibrium mixture however. The cis-trans ratio of the methyl 4-methylthio-2-butenoates should be similar to that for crotonic acid, in which the trans isomer is heavily favored (57). No trace of this isomer was found experimentally.

A preliminary investigation was carried out in which g.l.c. was considered as an analytical method. Columns such as PDEAS, SE 30, and diisodecyl phthalate are capable of effecting partial resolution of the three principal isomers. The best column in terms of resolution was found to be the PDEAS column but unfortunately the samples underwent further isomerization during the g.l.c. analysis itself.

The n.m.r. spectra of the three isomers in nonpolar solvents such as carbon tetrachloride and carbon disulfide show that the singlets due to the methylthio groups are sufficiently separated to allow determination of the integrated area under each spectral curve. The ratio of these areas give a direct measure of the concentration ratio of the three isomers. The desired equilibrium constants are dimensionless so it is not

57. A. L. Markman and E. V. Zinkova, Zhur. Obshch. Khim., 29, 2362 (1952).

necessary to determine the absolute concentration of each isomer. One can also obtain the mole fraction of the methyl trans-4-methylthio-2-butenoate by using the singlets due to the methoxy groups. The methoxy singlets of cis and trans methyl 4-methylthio-3-butenoate are accidentally degenerate, only the sum of their areas can be obtained, but the methoxy singlet of methyl trans-4-methylthio-2-butenoate is resolved towards lower field. In this case, the mole fraction of methyl trans-4-methylthio-2-butenoate is obtained by dividing the area of the methoxy singlet at lower field by the total area of both. Less confidence is placed in this value because the resolution is not as good as that of the methylthio singlets.

The equilibration solution was prepared by adding 1.00 ml. of esters, 5.00 ml. of tert-butyl alcohol, and 0.25 ml. of distilled triethylamine to a flask fitted with a septum. This was then placed in a 35.0° bath at time zero and 0.625 ml. samples were withdrawn by syringe at various times. The samples were run into a centrifuge tube with septum containing 0.40 ml. of carbon disulfide and 6.00 ml. of pH 7 buffer solution to which had been added sufficient hydrochloric acid to neutralize the triethylamine in the sample. After shaking, the extract was centrifuged and the lower layer was transferred to a thin walled n.m.r. tube. The spectrum was recorded using a sweep rate of 0.40 cycles per second, a sweep width of 100 cycles, a filter band width setting of four, and a RF field of 0.04 milliguss. The areas were determined using a planimeter and by electrical integration.

Three runs were made in which the original concentration of a

different one of the three isomers was greater than its value at equilibrium (i.e., the equilibrium was approached from three directions). The results of the equilibrations are found in Table 4. The

Table 4. Equilibration of the Methyl 4-Methylthiobuteneoates at 35° in tert-Butyl Alcohol.

0.88 M Ester 0.29 M Triethylamine

Time (hours)	Mole Per Cent				Integration	
	cis-$\beta\gamma$	trans-$\beta\gamma$	trans-$\alpha\beta$	trans-$\alpha\beta$[a]	Method[b]	Number
Run I						
0.0	3.0	12.7	84.4	87.5	P	2, 1[a]
2.0	11.3	7.7	81.0		P	1
20.3	25.4	30.8	43.7	43.2	P	1, 2[a]
65.3	23.8	30.9	45.3	40.4	P	3, 2[a]
115.3	27.0	33.3	39.6	38.7	P	4, 3[a]
	23.7	33.6	42.7		E	13
137.3	29.0	33.1	37.8	41.7	P	3, 1[a]
	24.1	33.8	42.0	41.4	E	13, 15[a]
Run II						
0.0	59.3	7.2	33.5		P	1
16.3	28.9	25.0	46.2	44.7	P	3, 3[a]
61.0	24.8	33.8	41.3	41.0	P	3, 2[a]
119.0	23.4	34.6	42.0	39.2	P	4, 2[a]
	24.0	33.7	42.3		E	20
133.0	24.3	33.3	42.2	43.4	P	2, 1[a]
	23.8	34.0	42.1	41.1	E	10, 13[a]
Run III						
0.0	15.0	73.6	11.4	13.3	P	2, 2[a]
119.3	24.0	33.6	42.4		E	15
133.0	23.8	33.9	42.2	41.6	E	14, 12[a]

[a] This data is based on the methoxy singlets.

[b] P indicates use of a planimeter and E indicates use of an electrical integrator.

isomer ratios of the extract was shown to be the same as that in the equilibration solution by re-extracting the aqueous layer and comparing the n.m.r. response of each isomer with that of the first extract.

The calculated extraction efficiencies in the first extraction were found to be 0.924, 0.926, and 0.927 for the cis-$\beta\delta$, trans-$\beta\delta$, and trans-$\alpha\beta$ isomers respectively. The data expressed in Table 4 require no correction for this factor.

The stability of esters in the equilibrated solution and in the extracts themselves was verified by the observation that no significant decrease in the n.m.r. response was noted for the samples after standing for several days. No significant bands were noted in the extract of the equilibrated solution other than those due to the three isomers or to the tert-butyl alcohol.

Isomerization of Methyl 4-Methoxycrotonate

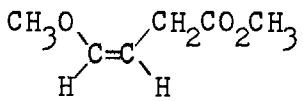
Isomerization of methyl 4-methoxycrotonate produces selectively methyl cis-4-methoxy-3-butenoate when carried out in tert-butyl alcohol using potassium methoxide as catalyst. If methanol is used as solvent another compound is formed which is thought to be methyl 3,4-dimethoxybutenoate. The equilibrium constant for addition of methanol to methyl

cis-4-methoxy-3-butenoate was estimated in order to determine the methanol concentration which would largely eliminate this component from the equilibrium mixture.

The specific responses of methyl 3,4-dimethoxybutenoate and methyl cis-4-methoxy-3-butenoate were determined with g.l.c. instrument number

1 using a PDEAS column at 170° and were found to be 778 ± 25 mm^2/mg. and 727 ± 20 mm^2/mg. respectively[1]. The retention times observed were 4.7 minutes for methyl cis-4-methoxy-3-butenoate, and 6.7 minutes for methyl 3,4-dimethoxybutenoate.

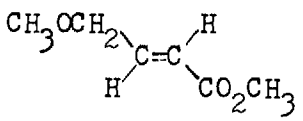
A methanol solution was prepared which contained 0.063 M sodium methoxide, 1.2 M methyl 4-methoxycrotonate, 19 M methanol, and 4.0 volume per cent of mesitylene, as internal standard. This solution was placed in the 35.0° bath for one day. A sample was taken, neutralized with methanolic hydrogen chloride, and examined on the g.l.c. instrument as above. The peak areas at indicated retention times were: 145 mm^2 (4.7 min.), 7.4 mm^2 (5.4 min.), 5.4 mm^2 (5.8 min.), and 461 mm^2 (6.7 min.). The peak at 5.4 minutes may be due to the methyl trans-4-methoxy-3-butenoate and the one at 5.8 minutes is due to methyl 4-methoxycrotonate. If one assumes that the specific responses and the molecular weights are the same for the compounds having retention times of 4.7, 5.4, and 5.8 minutes, the relative molar concentrations are calculated to be:



1.00

Unknown Compound

ca. 0.051



ca. 0.037

$CH_3OCH_2CH(OCH_3)CH_2CO_2CH_3$

2.36

The time used (one day) was ample to insure equilibrium since a steady state was reached in about five hours.

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[1] Areas were estimated as peak height times the width at half height.

A similar experiment was carried out using a tert-butyl alcohol solution containing 0.10 M sodium methoxide, 0.62 M methyl 4-methoxycrotonate, 1.02 M methanol, and 4.0 volume per cent of mesitylene. The rate of this reaction was followed at 20° and the equilibrium concentrations were finally measured at 35.0°. The procedure and the assumptions were the same as before except the samples were quenched with pH 7 buffer solution (the maximum resulting pH after neutralization was estimated to be 7.4) and then extracted with chloroform (shown to be greater than 99 per cent efficient). The results of this experiment are presented in Table 5.

Table 5. Isomerization of Methyl 4-Methoxycrotonate in tert-Butyl Alcohol at 20° and 35.0°.

0.10 M Sodium Methoxide 0.62 M Ester

1.02 M Methanol

Time at 20° (seconds)	Mole Fraction				
	cis-β,δ	trans-α,β	Methanol Adduct	Unknown Compound[a]	Total
0	0.000	1.000	0.000	0.000	1.000
80	0.103	0.717	0.178	-	0.998
150	0.164	0.550	0.280	-	0.994
225	0.201	0.420	0.335	< 0.013	0.967
405	0.263	0.251	0.420	< 0.036	0.970
8000	0.585	0.044[a]	0.210	0.07	0.909
3000 at 35.0°[b]	0.610	0.090[a]	0.109	0.07	0.879

[a] Values are based on absolute peak heights. The poor resolution obtained causes an error which makes these values to high.

[b] The sample had been at 20° for 8000 seconds prior to this.

From these data the equilibrium constant at 35.0° for the addition of methanol to methyl cis-4-methoxy-3-butenoate is estimated to be 0.13 l/mole in methanol and 0.19 l/mole in tert-butyl alcohol. A nineteen-fold variation in the concentration of methanol was made between the two determinations. The maximum permissible methanol concentration which will keep the mole fraction of the addition compound below 0.01 is about 0.06 M. Sodium methoxide is sparingly soluble in tert-butyl alcohol and the procedure of diluting concentrated solutions of sodium methoxide in methanol with tert-butyl alcohol is not desirable here.

The problem of obtaining a reasonable concentration of methoxide ion in tert-butyl alcohol was solved by treating solutions of potassium tert-butoxide in tert-butyl alcohol with the calculated amount of methanol to form potassium methoxide. A reasonably stable, supersaturated solution of 0.2 M potassium methoxide in tert-butyl alcohol can be prepared by this method.

The equilibrium between methyl 4-methoxycrotonate and methyl cis-4-methoxy-3-butenoate was studied using n.m.r. spectroscopy as the analytical method. The isomerization cannot be followed in situ since the methoxy singlets are unrelolved in tert-butyl alcohol. However, in carbon disulfide solution the methoxy singlets of methyl 4-methoxy-crotonate are found 4.2 cycles to the left (higher field) and 15.6 cycles to the right (lower field) of the unresolved methoxy singlets of methyl cis-4-methoxy-3-butenoate. Integration of these singlets give a measure of the relative amounts of each isomer in the carbon disulfide solution.

The equilibration was carried out by preparing a tert.-butyl alcohol solution containing 0.209 M potassium methoxide and 1.02 M methyl 4-methoxycrotonate and placing this in the 35.0° bath. At time intervals 0.625 ml. samples were withdrawn and run into a centrifuge tube fitted with a septum and containing 0.40 ml. of carbon disulfide 0.60 ml. of pH 7 buffer, and sufficient hydrochloric acid to neutralize the potassium methoxide. The mixture was shaken and centrifuged. The lower layer was then examined using n.m.r. spectroscopy. It was necessary to multiply the determined fraction [methyl 4-methoxycrotonate]/[methyl cis-4-methoxy-3-butenoate] by a factor of 1.15 in order to correct for the unequal extraction of the two isomers. This factor was determined by comparing the n.m.r. response of a first and second extract.

Comparison of the areas of the methoxy singlets was not very accurate as the equilibration neared completion since the spectrum amplitued had to be reduced in order to keeep the unresolved methoxy singlets "on scale." This was rectified by using the methylene proton absorption of methyl cis-methoxy-3-butenoate (a doublet split into doublets) as a measure of its relative concentration. The results of the equilibration are given in Table 6.

Isomerization of the 1-Methoxypropynes and Methoxyallene

Base catalyzed isomerization of 3-methoxypropyne can conceivably produce methoxyallene and 1-methoxypropyne. The equilibration was carried out in dimethyl sulfoxide solution using dimsylsodium as base.

The progress of the reaction was followed *in situ* by n.m.r. spectroscopy since the bands of the three compounds are well resolved in

Table 6. Equilibration of Methyl 4-Methoxycrotonate in tert-Butyl Alcohol at 35.0°.

0.209 M Potassium Methoxide 1.02 M Ester

Time (Seconds)	Mole Per Cent Methyl 4-Methoxycrotonate[a]	
	Method I[b]	Method II[c]
0	100.0	
40	58.0	
100	28.7	
400	4.6	5.16
1000	1.5	2.13
3000		1.91
3020		1.99

[a] Balance is methyl cis-4-methoxy-3-butenoate. Corrected for extraction.

[b] Based on the ratio of the methoxy singlets

[c] Based on the methoxy singlets of methyl 4-methoxycrotonate and the methylene absorption of methyl cis-4-methoxy-3-butenoate.

dimethyl sulfoxide. The singlets due to the methoxy groups allow detection of trace amounts of each isomer down to about one per cent of the total concentration of isomers. A solution of 1.02 ml. of 0.05 M dimsylsodium and 0.030 ml. of 3-methoxypropyne was placed in a n.m.r. tube and the spectrum recorded. Conversion to methoxyallene at room temperature was found to be 50 per cent complete in ten hours. The base concentration was then increased 0.06 M by addition of 0.030 ml. of 2.3 M dimsylsodium in dimethyl sulfoxide. After three days at room temperature the ratio of

methoxyallene to 3-methoxypropyne was about 100:1. No 1-methoxypropyne was ever observed during this time or for several days afterwards which suggests a ratio of methoxyallene to 1-methoxypropyne of greater than 100:1.

The possibility that methoxyallene is the thermodynamically most stable isomer was explored by attempting to isomerize 1-methoxypropyne to methoxyallene. The n.m.r. spectrum of a solution of 0.030 ml. of 1-methoxypropyne and 1.02 ml. of 0.05 M dimsylsodium in dimethyl sulfoxide was found to remain unchanged after ten hours at room temperature and after 30 minutes at 100°. Increasing the base concentration 0.06 M by adding 0.030 ml. of 2.3 M of dimsylsodium in dimethyl sulfoxide and heating at 100° for 85 minutes resulted in consumption of about one half of the 1-methoxypropyne without producing any distinct new bands in the n.m.r. spectrum of the sample. It is possible in this case that a ratio of 1-methoxypropyne to methoxyallene of about 50:2 might have gone undetected.

Attempted Equilibration of 3,3-Dimethoxy-1-propene and 1,1-Dimethoxy-1-propene

A solution of 0.221 g. of 3,3-dimethoxypropene and 1.19 g. of 0.35 M potassium tert-butoxide in dimethyl sulfoxide was sealed in an n.m.r. tube and allowed to stand two days at room temperature. The n.m.r. spectrum of the initial sample showed a broad multiplet 180 c.p.s. up field of the dimethyl sulfoxide singlet[1] due to the vinyl

[1] Chemical shifts are given relative to the dimethyl sulfoxide singlet throughout this section.

protons, a doublet (J = 4 c.p.s.) split into triplets (J = 1.4 c.p.s.) 130 c.p.s. upfield due to the carbon 3 proton, and a singlet 40 c.p.s. upfield due to the methoxy protons (the relative areas were ca. 3, 1, and 6 respectively). The sample showed no change in its n.m.r. spectrum after standing for two days at room temperature, but heating to 55° for twelve hours produced some new bands. An apparent doublet (J = 2.5 c.p.s.) appeared 58 c.p.s. upfield, a doublet (J = 6.5 c.p.s.) appeared 65 c.p.s. downfield, and some lesser bands appeared 70 c.p.s. upfield. The first two bands were probably due to the methoxy protons and the carbon 3 protons of 1,1-dimethoxypropene since they were also present in the n.m.r. spectrum of a partially polymerized sample of 1,1-dimethoxypropene in dimethyl sulfoxide. The ratio of 3,3- to 1,1-dimethoxypropene was estimated to be approximately 20:1 after twelve hours at 55° based on the integrated areas of the absorptions due to the methoxy protons. This ratio did not appear to change on heating the sample at 55° for ten more hours.

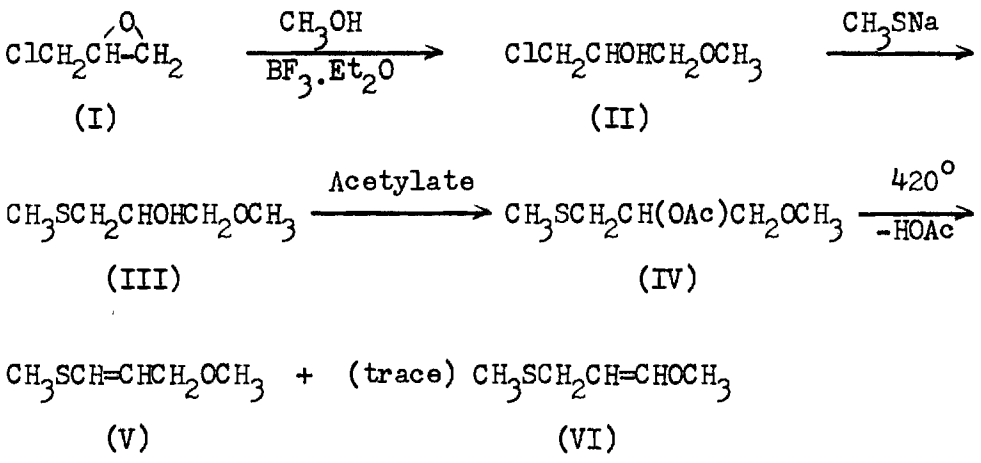
Although the sample of 1,1-dimethoxypropene had polymerized to an extent of about 60 per cent (This estimate was based upon the relative areas of the absorptions due to the methoxy protons. Since the polymer shows a strong singlet 35 c.p.s. upfield) an attempt was made to isomerize the remaining olefin. A solution of 0.217 g. of partially polymerized 1,1-dimethoxypropene and 1.11 g. of 0.35 M base solution was heated in an n.m.r. tube for twenty hours at 55°. No noticeable change in the n.m.r. spectrum was found after this treatment. In view of this result the study was discontinued.

CHAPTER III

Results and Discussion

Syntheses of Olefins

An acetate pyrolysis was employed for the preparation of 3-methoxy-1-methylthiopropene (V). Using boron trifluoride etherate as catalyst, methanolysis of epichlorohydrin (I) gave 1-chloro-2-hydroxy-3-methoxypropane (II), which was converted to the sulfide (III) by the action of sodium methyl mercaptide. The sulfide (III) was acetylated affording the 2-acetate (IV). The acetate (IV) eliminated acetic acid at 420° in the gas phase to give the vinyl sulfide (V) and only one or



two per cent of the vinyl ether (VI). Careful distillation of the vinyl sulfide (V) gave partial resolution of the *cis* and *trans* isomers.

Attempts to prepare the sulfide (V) by elimination of methyl mercaptan from a mercaptal (39) were unsuccessful. The mercaptal (VIII) was prepared from the acetal (VII) and methyl mercaptan using a trace of methanolic hydrogen chloride as catalyst. Pyrolysis of the mercaptal in the presence of a trace of acid gave no detectable vinyl sulfide (V), but gave instead, a compound thought to be the sulfide (IX).

$$CH_3OCH_2CH_2CH(OCH_3)_2 \xrightarrow[-2CH_3OH]{2CH_3SH} CH_3OCH_2CH_2CH(SCH_3)_2 \xrightarrow[245^\circ]{H^+}$$

(VII) (VIII)

$$CH_3SCH{=}CHCH_2SCH_3 + CH_3OH$$

(IX)

Preparations of vinyl sulfides have been accomplished by the addition of thiols to acetylenes (58), so the reaction between methyl propargyl ether (X) and methyl mercaptan was investigated. The reaction was tried

$$CH_3OCH_2C{\equiv}CH + CH_3SH \xrightarrow[(BzO)_2]{h\nu} CH_3OCH_2CH(SCH_3)CH_2SCH_3$$

(X) (XI)

$$+ CH_3OCH_2CH{=}CHSCH_3$$

(V)

with benzoyl peroxide, with ultraviolet light, and with both. The main product of the reaction was the di-addition compound (XI); only minor

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58. A. A. Oswald, K. Griesbaum, B. E. Hudson, Jr., J. M. Bregman, J. Am. Chem. Soc., 86, 2877 (1964).

amounts of the mono-addition compound (V) were obtained. A similar result was observed (59) when thiolacetic acid was added to methyl propargyl ether (X).

Synthesis of 1-methoxy-3-methylthiopropene (XIV) was accomplished by the general procedure of dehydrohalogenation of an alpha-chloro ether (60). Triethyl amine catalyzed addition of methyl mercaptan to acrolein gave the aldehyde (XII). The aldehyde was converted to the alpha-chloro ether (XII) by the action of methanolic hydrogen chloride. The ether

$$CH_2{=}CHCHO + CH_3SH \xrightarrow{Et_3N} \underset{(XII)}{CH_3SCH_2CH_2CHO} \xrightarrow[CH_3OH]{HCl}$$

$$\underset{(XIII)}{CH_3SCH_2CH_2CHClOCH_3} \xrightarrow{PhN(CH_3)_2} \underset{(XIV)}{CH_3SCH_2CH{=}CHOCH_3}$$

(XIII) was not isolated due to the instability of such compounds; but rather was converted to the vinyl ether (XIV) using N,N-dimethyl aniline. The cis and trans isomers of the vinyl ether were separated by preparative g.l.c.

A less useful preparation of the vinyl ether (XIV) utilized elimination of methanol from an acetal (43). Acrolein was treated with methanolic hydrogen chloride giving the chloro acetal (XV), which was

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59. H. Bader, L. C. Cross, Sir Ian Heilbron, and E. R. H. Jones, J. Chem. Soc., 619 (1949).

60. H. R. Warner and W. E. M. Lands, J. Am. Chem. Soc., 85, 60 (1963).

then converted to the sulfide (XVI). Elimination of methanol from the

$$CH_2{=}CHCHO \xrightarrow[HCl]{CH_3OH} ClCH_2CH_2CH(OCH_3)_2 \xrightarrow{CH_3SNa}$$

(XV)

$$CH_3SCH_2CH_2CH(OCH_3)_2 \xrightarrow[-CH_3OH]{175^\circ} CH_3SCH_2CH{=}CHOCH_3$$

(XVI) (XIV)

sulfide (XVI) was effected by pyrolysis, probably an acid catalyzed reaction, to produce the vinyl ether (XIV) in low yield.

Preparation of trans-1-methoxy-4-methylthio-2-butene (XIX) was accomplished by successive displacement reactions upon trans-1,4-dichloro-2-butene (XVII). The reaction of one equivalent of sodium methoxide with the dichloro compound (XVII) gave a mixture of the dichloro (XVII), chloro-methoxy, and dimethoxy (XVIII) compounds, which could not be separated by distillation. However, further reaction of the mixture with one equivalent of sodium methyl mercaptide gave a mixture of the dimethoxy (XVIII), methoxy-methylthio (XIX), and dimethylthio (XX) compounds, which was easily separated by distillation.

$$\underline{\text{trans}}\ ClCH_2CH{=}CHCH_2Cl \xrightarrow[2)\ CH_3SNa]{1)\ CH_3ONa} \underline{\text{trans}}\ CH_3OCH_2CH{=}CHCH_2OCH_3$$

(XVII) (XVIII)

$$+\ \underline{\text{trans}}\ CH_3OCH_2CH{=}CHCH_2SCH_3 + \underline{\text{trans}}\ CH_3SCH_2CH{=}CHCH_2SCH_3$$

(XIX) (XX)

Methyl propargyl ether (XXI) was prepared by alkylation of propargyl alcohol with dimethyl sulfate. The ether was isomerized, using

$$HOCH_2C{\equiv}CH \xrightarrow[NaOH]{(CH_3O)_2SO_2} \underset{(XXI)}{CH_3OCH_2C{\equiv}CH} \xrightarrow[(CH_3)_2SO]{CH_3ONa} \underset{(XXII)}{CH_3OCH{=}C{=}CH_2}$$

sodium methoxide in dimethyl sulfoxide, giving methoxyallene (XXII).

The general method (61) of alkylation of a sodium alkoxyacetylide was used for the synthesis of 1-methoxypropyne (XXIII). Dimethyl chloroacetal was treated with two equivalents of sodium amide in liquid ammonia and the resulting sodium methoxyacetylide was alkylated with

$$ClCH_2CH(OCH_3)_2 \xrightarrow[2)\ CH_3I]{1)\ 2NaNH_2} \underset{(XXIII)}{CH_3OC{\equiv}CCH_3}$$

methyl iodide giving 1-methoxypropyne (XXIII) in rather low yield. It was difficult to recover the low boiling ether (XXIII) from the large amount of liquid ammonia used as solvent.

The methoxy (47) and methylthio (48) substituted methyl crotonates were prepared in the following manner. Crotonic acid, a trans compound, was brominated with N-bromosuccinimide, NBS, to give the 4-bromo ester

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61. L. Brandsma and J. F. Arens, Rec. Trav. Chim., 81, 510 (1962).

(XXIV). Methanolysis of the 4-bromo ester in the presence of calcium

$$\underline{\text{trans}}\ CH_3CH{=}CHCO_2H \xrightarrow[CH_3OH]{H^+} \underline{\text{trans}}\ CH_3CH{=}CHCO_2CH_3 \xrightarrow[(BzO)_2]{NBS}$$

$$\underline{\text{trans}}\ BrCH_2CH{=}CHCO_2CH_3 \xrightarrow[CaCO_3]{CH_3OH} \underline{\text{trans}}\ CH_3OCH_2CH{=}CHCO_2CH_3$$

(XXIV) (XXV)

$$\xrightarrow[(CH_3)_3COH]{CH_3ONa} \underline{\text{cis}}\ CH_3OCH{=}CHCH_2CO_2CH_3$$

(XXVI)

carbonate affords methyl trans-4-methoxy-2-butenoate (XXV), which is isomerized to methyl cis-4-methoxy-3-butenoate (XXVI) by sodium methoxide in tert-butyl alcohol. The 4-bromo ester (XXIV) is converted to methyl trans-4-methylthio-2-butenoate (XXVII) by treatment with methyl mercaptan

$$\underline{\text{trans}}\ BrCH_2CH{=}CHCO_2CH_3 \xrightarrow[(C_2H_5)_3N]{CH_3SH} \underline{\text{trans}}\ CH_3SCH_2CH{=}CHCO_2CH_3$$

(XXIV) (XXVII)

and triethylamine. Isomerization of the ester (XXVII) by heating with triethylamine at 100° gives a mixture of the esters (XXVII), (XXVIII), and (XXIX), which can be separated by preparative g.l.c.

$$\underline{\text{trans}}\ CH_3SCH_2CH{=}CHCO_2CH_3 \xrightarrow{(C_2H_5)_3N} \underline{\text{cis}}\ \text{and}\ \underline{\text{trans}}\ CH_3SCH{=}CHCH_2CO_2CH_3$$

(XXVII) (XXVIII) and (XXIX)

Synthesis of 1,1-dimethoxypropene (XXXIII) was accomplished by a procedure used for the preparation of 1,1-diethoxyethylene (55). This procedure has been used by McElvain (54) for the preparation of 1,1-dimethoxypropene (XXXIII), but the results are unpublished as yet. Propionitrile was converted to trimethyl orthopropionate (XXXI) by means of the imidoester hydrochloride (XXX). The orthoester (XXXI) was brominated giving the bromo compound (XXXII), which was demethoxy-

$$CH_3CH_2CN \xrightarrow[CH_3OH]{HCl} \underset{(XXX)}{CH_3CH_2C(OCH_3)=NH\cdot HCl} \xrightarrow{CH_3OH} \underset{(XXXI)}{CH_3CH_2C(OCH_3)_3}$$

$$\xrightarrow{Br_2} \underset{(XXXII)}{CH_3CHBrC(OCH_3)_3} \xrightarrow{Na} \underset{(XXXIII)}{CH_3CH=C(OCH_3)_2}$$

brominated affording 1,1-dimethoxypropene (XXXIII).

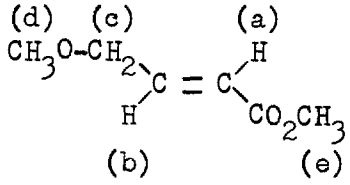
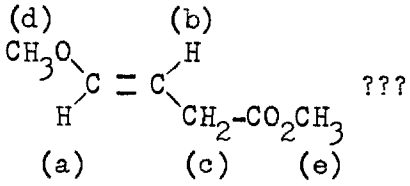
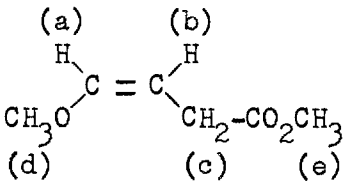
Assignment of Structure

Nonsterospecific syntheses were generally used in the preparations of the various olefins and it was necessary to assign structures by means of n.m.r. and infrared spectroscopy.

Nuclear Magnetic Resonance Spectroscopy

Tables 7, 8, 9, and 10 contain a summary of the n.m.r. data for the various isomeric olefins. Among the vinyl sulfides and vinyl ethers the coupling constants for the vinyl protons are internally consistent. For the vinyl sulfides J_{trans} is about 14.8 c.p.s. and J_{cis} is about 9.6 c.p.s. The vinyl ethers have slightly smaller values; J_{trans} is about

Table 7. NMR Data for Isomers of Methyl 4-Methoxycrotonate in 50 per cent Carbon Tetrachloride.

Compound	Coupling Constant (c.p.s.)	Chemical Shift (τ)	Area
	Jab = 15.6	a) 4.00	0.97
	Jac = 2.0	b) 3.08	1.03
	Jbc = 4.1	c) 5.93	2.01
		?d) 6.63	3.01
		?e) 6.29	2.98
 ???	Jab = 13	a) 3.67	0.9
	Jac = 1.2	b) 5.28	1.1
	Jbc = 7.2	c) 7.13	1.8
		?d) 6.36	3.4
		?e) 6.48	2.7
	Jab = 6.5	a) 3.98	0.94
	Jac = 1.6	b) 5.50	1.03
	Jbc = 6.9	c) 6.95	1.97
		?d) 6.40	2.98[a]
		?e) 6.42	3.08[a]

[a] These peaks are resolved in the neat liquid.

Table 8. NMR Data for Isomers of Methyl 4-Methylthiocrotonate in 50 per cent Carbon Tetrachloride.

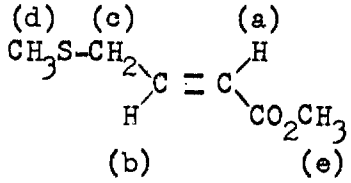
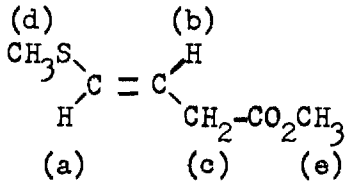
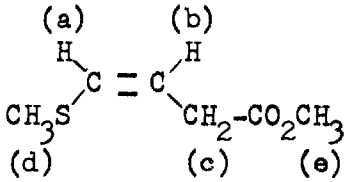
Compound	Coupling Constant (c.p.s.)	Chemical Shift (τ)	Area
	Jab = 15.4	a) 4.13	0.89
	Jac = 1.0	b) 3.17	0.84
	Jbc = 7.6	c) 6.76	2.08
		d) 7.99	3.10
		e) 6.31	3.11
	Jab = 14.6	a) 4.06	0.97
	Jac < 1.0	b) 4.80	0.96
	Jbc = 6.7	c) 7.06	1.88
		d) 7.84	3.15
		e) 6.48	2.96
	Jab = 9.5	a) 3.89	0.94
	Jac = 1.3	b) 4.36	0.92
	Jbc = 6.7	c) 6.90	2.00
		d) 7.73	2.98
		e) 6.38	3.01

Table 9. NMR Data for cis and trans 1-Methoxy-3-methylthiopropene in 50 per cent Carbon Tetrachloride.

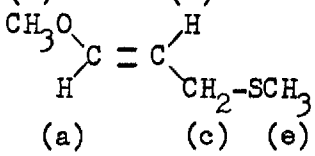
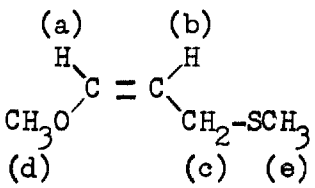
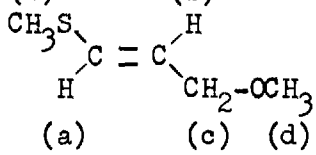
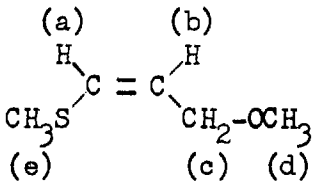
Compound	Coupling Constant (c.p.s.)	Chemical Shift (τ)	Area
	Jab = 12.5	a) 3.64	0.94
	Jac ≈ 0.8	b) 5.33	1.00
	Jbc = 7.7	c) 7.02	1.92
		d) 6.49	3.00
		e) 8.04	3.03
	Jab = 6.0	a) 3.99	0.98
	Jac = 1.0	b) 5.64	1.02
	Jbc = 8.0	c) 6.93	1.93
		d) 6.44	3.10
		e) 8.03	2.96

Table 10. NMR Data for cis and trans 3-Methoxy-1-methylthiopropene in 50 per cent Carbon Tetrachloride.

Compound	Coupling Constant (c.p.s.)	Chemical Shift (τ)	Area
	Jab = 15.0	a) 3.72	0.90
	Jac = 1.0	b) 4.61	0.91
	Jbc = 6.0	c) 6.12	1.85
		d) 6.76	3.25
		e) 7.78	3.13
	Jab = 9.8	a) 3.95	0.92
	Jac = 1.3	b) 4.43	0.98
	Jbc = 6.0	c) 6.07	1.97
		d) 6.76	3.15
		e) 7.77	3.00

12.8 c.p.s. and J_{cis} is about 6.2 c.p.s. This is in qualitative agreement with the coupling constants observed (20) for methyl vinyl sulfide (J_{trans} = 16.4 c.p.s., J_{cis} = 10.3 c.p.s.) and methyl vinyl ether (J_{trans} = 14.1 c.p.s., J_{cis} = 7.0 c.p.s.). The coupling constants of the vinyl protons of methyl styryl sulfide are similar (58); J_{trans} is 15.5 c.p.s. and J_{cis} is 11.2 c.p.s. For methyl 1-dodecenyl ether J_{trans} is about 12.5 c.p.s. and J_{cis} is about 6.5 c.p.s. (41). Generally it is observed that trans coupling constants are in the range 11 to 18 c.p.s. and cis coupling constants are in the range 6 to 14 c.p.s. (62).

Infrared Spectrometery

Disubstituted ethylenes have trans vinyl protons generally give rise to medium to strong bands at 965 to 990 cm^{-1} and when the double bond is conjugated with a carbonyl group the absorption occurs in the range 974 to 980 cm^{-1} (63). When these protons are cis the position of this band due to out-of-plane hydrogen deformation is more variable, but it is generally near 700 cm^{-1} (63).

Table 11 summarizes the infrared spectra of the olefins and contains some reference compounds. In general it appears that cis vinyl ethers give rise to bands near 750 cm^{-1} while the trans isomers give rise to bands near 940 cm^{-1}. The vinyl ethers show at least two strong bands in the region in which C-O stretching absorptions are found, presumably due to contributions from a =CH-O and $-CH_2-O$ stretching mode

62. L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, New York, 1959, p. 85.

63. L. J. Bellamy, "The Infra-red Spectra of Complex Molecules," 2nd ed., Methuen and Co., London, 1958, p. 45.

Table 11. Summary of Infrared Spectra of Olefins

Compound	Isomer	Absorptions (cm^{-1})[a]				Ref.
		=CH- Out of Plane	C=O Stretch[b]	C-O Stretch[b]	C=C Stretch[b]	
$CH_3OCH=CHCH_2SCH_3$	cis	761		1113 1137 1215 1237	1650	
	trans	940		1137 1215 1237	1650	
$CH_3OCH=CHCH_2CO_2CH_3$	cis	758	1750	1112 1170 1200	1680	
$CH_3SCH=CHCH_2OCH_3$	cis	670		1120		
	trans	940		1120		
$CH_3SCH=CHCH_2CO_2CH_3$	cis	670	1750			
	trans	939	1750			
$CH_3SCH_2CH=CHCO_2CH_3$	trans	975 990?	1740			
$-HC=CHCO_2-$	trans	974-980	1717-1730			(63)
$-CH_2CO_2R$			1735-1750			(63)
$n-C_6H_{13}SCH=CHCH_3$	cis	661				(58)
	trans	934				(58)
$n-C_{10}H_{21}CH=CHOCH_3$	cis	735		1110 1260		(41)
	trans	930		1200 1170 1150 1125	1670	(41)

[a] Tentative assignments

[b] All are strong bands

(41). Those ethers of the type CH_3OCH_2R show only one strong band in this region, Table 11. The vinyl ethers show a strong band near 1670 cm^{-1}, due to C=C stretching, which is of considerable intensity in vinyl ethers (41).

The assignments in Table 11 are, of course, only tenative since in many cases other bands are located nearby.

Olefin Equilibria

The equilibrium studies are summarized in Table 12, in which the equilibrium mole per cent of each equilibrated isomer is reported. In general the data indicated the greater ability of methoxy groups to stabilize double bonds than either thiomethoxy or carbomethoxy groups.

Some isomers were either thermodynamically to unstable, e.g. the cis-2-butenoates, or not formed sufficiently rapid, e.g. methyl trans-4-methoxy-3-butenoate, to observe in the equilibrium mixtures. Those equilibria which involve an equilibrium concentration of one component of less than three mole per cent were only approached from the side of the least stable isomer (or isomers) but the fact that a steady state was attained in all cases indicates an equilibrium was obtained.

The failure to produce 1-methoxypropyne under conditions which isomerize methyl propargyl ether almost completely to methoxyallene shows that k_1 must be greater than k_2 by a factor greater than about one-thousand if 1-methoxypropyne is more stable than methoxyallene. On the other hand, if the latter order of stability is reversed, failure to produce methoxyallene from 1-methoxypropyne indicates $k_{-2} \ll k_1$. At any rate, 1-methoxypropyne was consumed by the action of base faster than it

was converted to methoxyallene. It may be that 1-methoxypropyne was consumed in a faster competing reaction in which dimsylsodium performed

$$CH_3OCH_2C{\equiv}CH \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} CH_3OCH{=}C{=}CH_2 \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} CH_3OC{\equiv}CCH_3$$

Table 12. Results of the Base-Catalyzed Equilibrations of Certain Olefins

Compound	T°	Solvent	Mole per cent at Equilibrium	
			cis	trans
$CH_3OCH_2CH{=}CHSCH_3$	50°	DMSO	ca. 1[a]	ca. 2[a]
$CH_3OCH{=}CHCH_2SCH_3$	50°	DMSO	31.6	65.5
$CH_3OCH_2CH{=}CHCO_2CH_3$	35°	tert-BuOH	—[b]	2.02[a]
$CH_3OCH{=}CHCH_2CO_2CH_3$	35°	tert-BuOH	98[a]	—[c]
$CH_3SCH_2CH{=}CHCO_2CH_3$	35°	tert-BuOH	—[b]	42.3
$CH_3SCH{=}CHCH_2CO_2CH_3$	35°	tert-BuOH	23.9	33.8
$CH_3OCH_2C{\equiv}CH$	ca. 25°	DMSO	ca. 1[a]	
$CH_3OCH{=}C{=}CH_2$	ca. 25°	DMSO	99[a]	
$CH_3OC{\equiv}CCH_3$	ca. 50°	DMSO	—[c]	

[a] Equilibrium values in as far as a steady state was attained.

[b] Thought to be to unstable to detect.

[c] Not formed due to kinetic control.

an S_N2 attack upon the methoxy carbon displacing an alkyneoxide anion.

$$CH_3S\bar{O}CH_2 + CH_3OC{\equiv}CCH_3 \longrightarrow CH_3SOCH_2CH_3 + \bar{O}C{\equiv}CCH_3$$

In this regard Arens and co-workers have generally used alkyl groups such as isopropyl and ethyl in their work with alkyl acetylenic ethers and sodium amide (64). These compounds should be much less reactive in such displacement reactions. Furthermore, the observation (64) that 1-alkynyl ethers, $RCH_2CH_2C{\equiv}COC_2H_5$, give low yields (30 to 40 per cent) of 1,3-enynes, $RCH{=}CHC{\equiv}CH$, by the action of sodium amide while 2-alkynyl ethers give high yields suggests a slow conversion of 1- to 2-alkynyl ethers. Considerable quantities of esters, $R(CH_2)_3CO_2C_2H_5$, acids, $R(CH_2)_3CO_2H$, and acid amides, $R(CH_2)_3CONH_2$, were found after acid hydrolysis of the reaction with 1-alkynyl ethers and it was suggested that these are possibly formed by addition of amide ion to the 1-alkynyl ether. The observation (27) that only trace amounts of alkoxyallenes are formed in the conversion by amide ion of 1-propynyl ethers to the salts of 2-propynyl ethers shows that 1-propynyl ethers cannot be much more stable than the alkoxyallenes.

The isomerization of 3,3-dimethoxypropene was attempted in dimethyl sulfoxide using potassium tert-butoxide as catalyst. Although about five mole per cent of 1,1-dimethoxypropene was probably produced it is not possible to say that this is the equilibrium value since the equilibrium

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64. P. P Montijn, H. M. Schmidt, J. H. van Boom, H. J. T. Bos, L. Brandsma, and J. F. Arens, Rec. Trav. Chim., 84, 271 (1965) and previous papers.

was not approached from the side of 1,1-dimethoxypropene.

The free energy change for isomerization of trans-3-methoxy-1-methylthiopropene to trans-1-methoxy-3-methylthiopropene is greater than 2.2 kcal/mole. It appears that a methoxy group would stabilize a double bond greater than 2.2 kcal/mole more than a thiomethoxy group would. Another way to estimate this value is to compare the equilibria of the substituted butenoates. If the thermodynamic cis-trans ratio of methyl 4-methoxy-3-butenoate is the same as that for 1-methoxy-3-methylthiopropene, the following can be written:

$$\frac{[\text{trans-}CH_3OCH{=}CHCH_2R]}{[\text{trans-}CH_3OCH_2CH{=}CHR]} = \frac{[\text{cis-}CH_3OCH{=}CHCH_2R][\text{trans-}CH_3OCH{=}CHR']}{[\text{trans-}CH_3OCH{=}CHCH_2R][\text{cis-}CH_3OCH{=}CHR']}$$

$$R = CO_2CH_3;\ R' = CH_2SCH_3$$

The value of (trans)/(cis) for 1-methoxy-3-methylthiopropene was found to be 2.02 at 50° and it should not differ much at 35°. Using this value, the above expression can be equated to 23.4 for the esters. This equilibrium constant corresponds to a change in free energy of -1.92 kcal/mole. On the other hand the isomerization of the corresponding thiomethoxy compound, trans to trans, has a free energy change of +0.137 kcal/mole. In this case it appears that the methoxy group stabilizes the double bond 2.06 kcal/mole more than the thiomethoxy group does.

The equilibrium concentration of 98 mole per cent methyl cis-4-methoxy-3-butenoate is somewhat surprising in view of the report that the equilibrium concentration of sodium 4-methoxy-2-butenoate (probably cis)

is 70 mole per cent relative to the crotonate (15). Since this type of equilibria is rather insensitive to the group (OR, O^-, or OH) which is attached to the carbonyl carbon (14) one might have expected a similar result.

In an unpublished study W. von E. Doering and R. Vollrath (65) have shown the methoxy group conjugatively interacts with a double bond to the extent of about 5.75 kcal/mole since equilibration of 1-methoxy-3-phenylpropene with potassium tert-butoxide in dimethyl sulfoxide at 26° gives 21.5 per cent of the 2-isomer and 78.5 per cent of the 1-isomer. The conjugative interaction of phenyl with the double bond was estimated to be about 5 kcal/mole. Data on the heats of hydrogenation of ethylene and ethyl vinyl ether suggest that RO stabilizes olefins more than hydrogen by 6.1 kcal/mole (17), while it appears that alkyl groups stabilize olefins about 2.5 kcal/mole more than hydrogen does (66). This data and the report (67) that the equilibration of methyl 2-hexenoate gives roughly 92 per cent of the 2-isomer and 8 per cent of the 1-isomer ($\Delta G \approx 1.6$ kcal/mole) can be used to predict a value of ΔG for the isomerization of methyl 4-methoxycrotonate to methyl cis-4-methoxy-3-butenoate of about -2.0 kcal/mole (-6.1 + 2.5 + 1.6) or -1.7 kcal/mole (-5.75 + 2.5 + 1.6). The observed value is -2.38 kcal/mole.

The equilibrium constant for conversion of methyl 4-methylthio-

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65. C. D. Broaddus, J. Am. Chem. Soc., 87, 3706 (1965).

66. J. E. Kilpatrick, E. J. Prosen, K. S. Pitzer, and F. D. Rossini, J. Res. Natl. Bur. Std., 36, 559 (1946).

67. G. A. R. Kon, R. P. Linstead, G. W. G. Maclennan, J. Chem. Soc., 2452 (1932).

crotonate to methyl trans-4-methylthio-3-butenoate is 0.80. Since the data in Table 1, entry 4, indicates CH_3S is slightly better, by a factor of 2, than C_3H_7 in stabilizing olefins, one might expect K to be 0.80/2 or about 0.4 for reactions like

$$R'\text{-}CH_2CR''{=}CHCO_2R''' \rightleftharpoons R'CH{=}CR''\text{-}CH_2CO_2R''' .$$

In a case already mentioned (R' = Et, R''' = H, R''' = Et) K is ca. 0.07 (67), while in another case (R' = Me, R'' = Me, R''' = Et) K is 0.33 (67). Note that if K is taken as 0.33 for this type of equilibria (ΔG = 0.7 kcal/mole) the earlier estimates of ΔG for the isomerization of methyl 4-methoxycrotonate to methyl cis-4-methoxy-3-butenoate would change to -2.9 kcal/mole and 2.6 kcal/mole which are in good agreement with the observed value of -2.38 kcal/mole.

CHAPTER IV

CONCLUSION

No evidence to support the hybridization effect was found in this work. The equilibrium between 1- and 3-methoxypropyne was not established but 3-methoxypropyne was converted to methoxyallene in ca. 99 per cent yield. The stabilization of olefins by a methoxy group was found to be about 2.0 to 2.2 kcal/mole more than by a thiomethoxy group.

APPENDIX

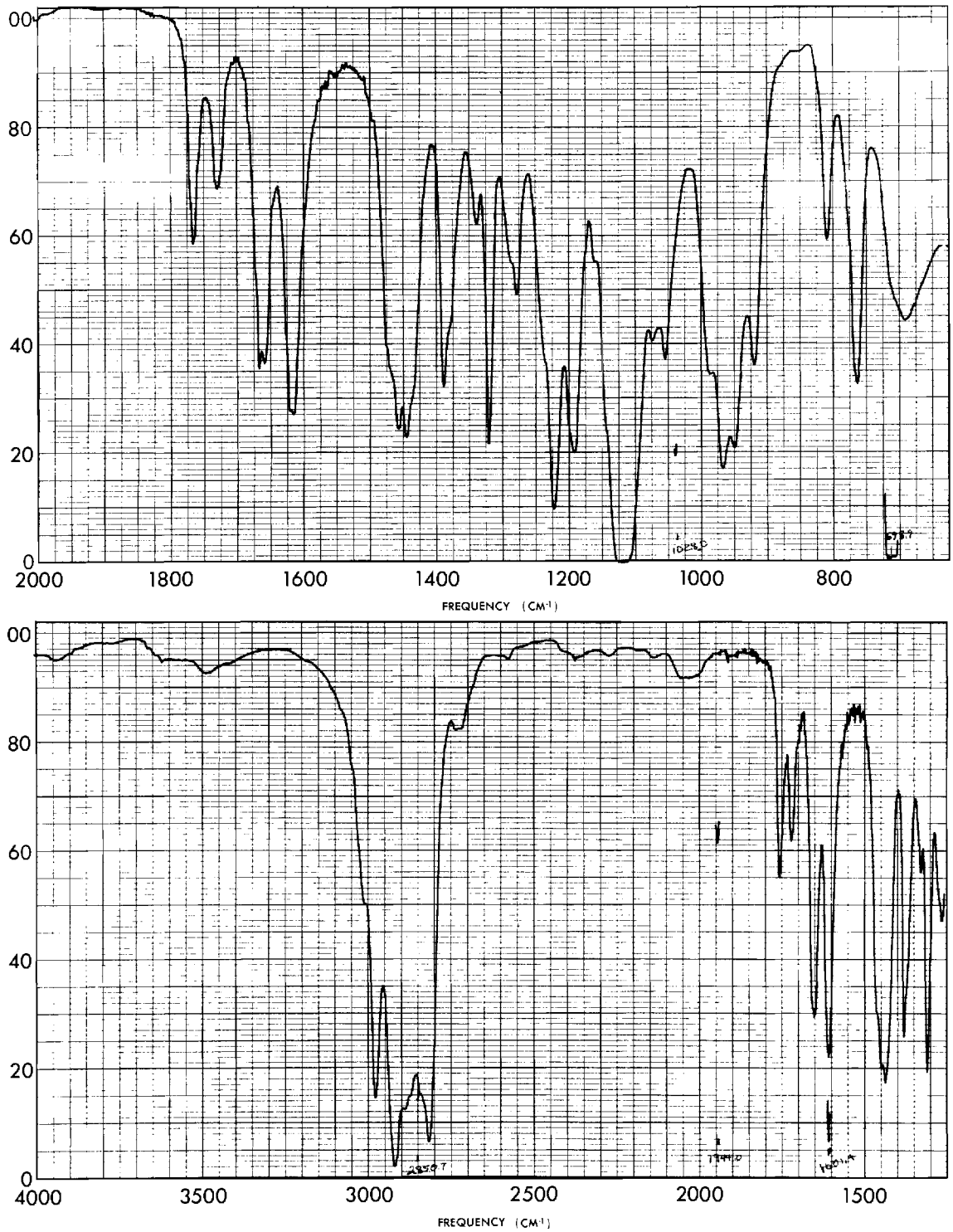

Figure 1. Infrared Spectrum of cis-3-Methoxy-1-methylthiopropene. (ca. 70 per cent cis and 30 per cent trans)

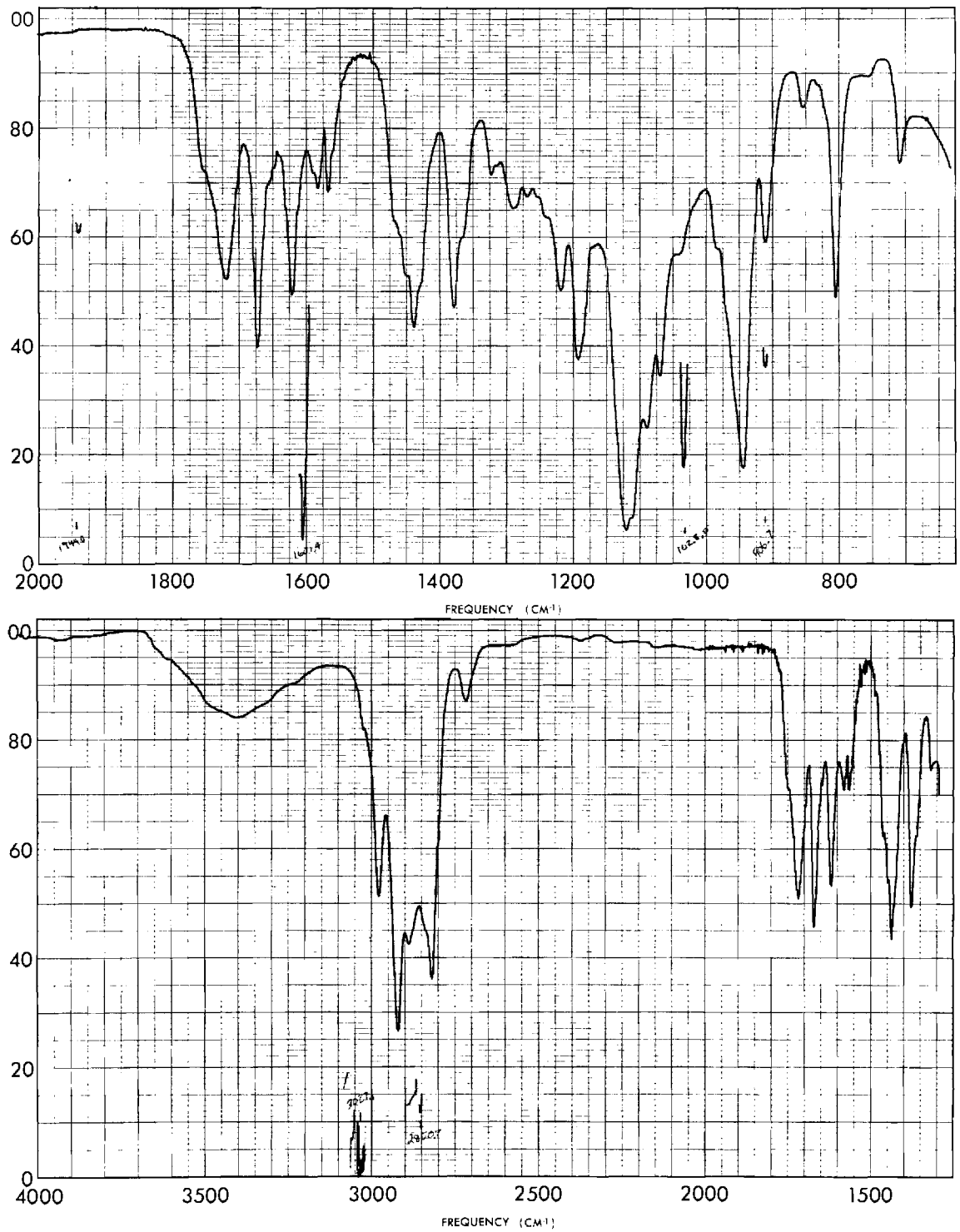

Figure 2. Infrared Spectrum of trans-3-Methoxy-1-methylthiopropene. (ca. 95 per cent trans and ca. 5 per cent cis)

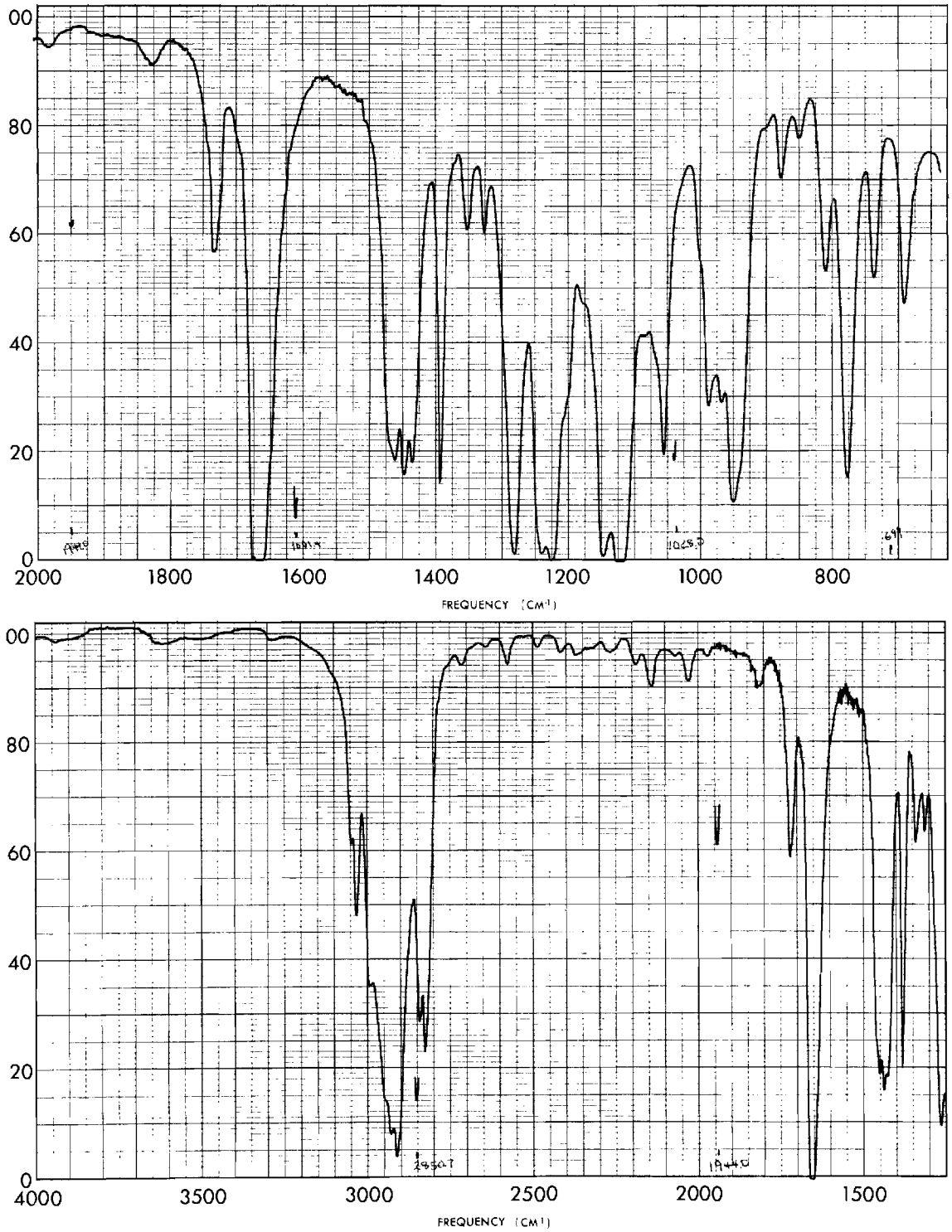

Figure 3. Infrared Spectrum of cis-1-Methoxy-3-methylthiopropene. (ca. 73 per cent cis and ca. 27 per cent trans)

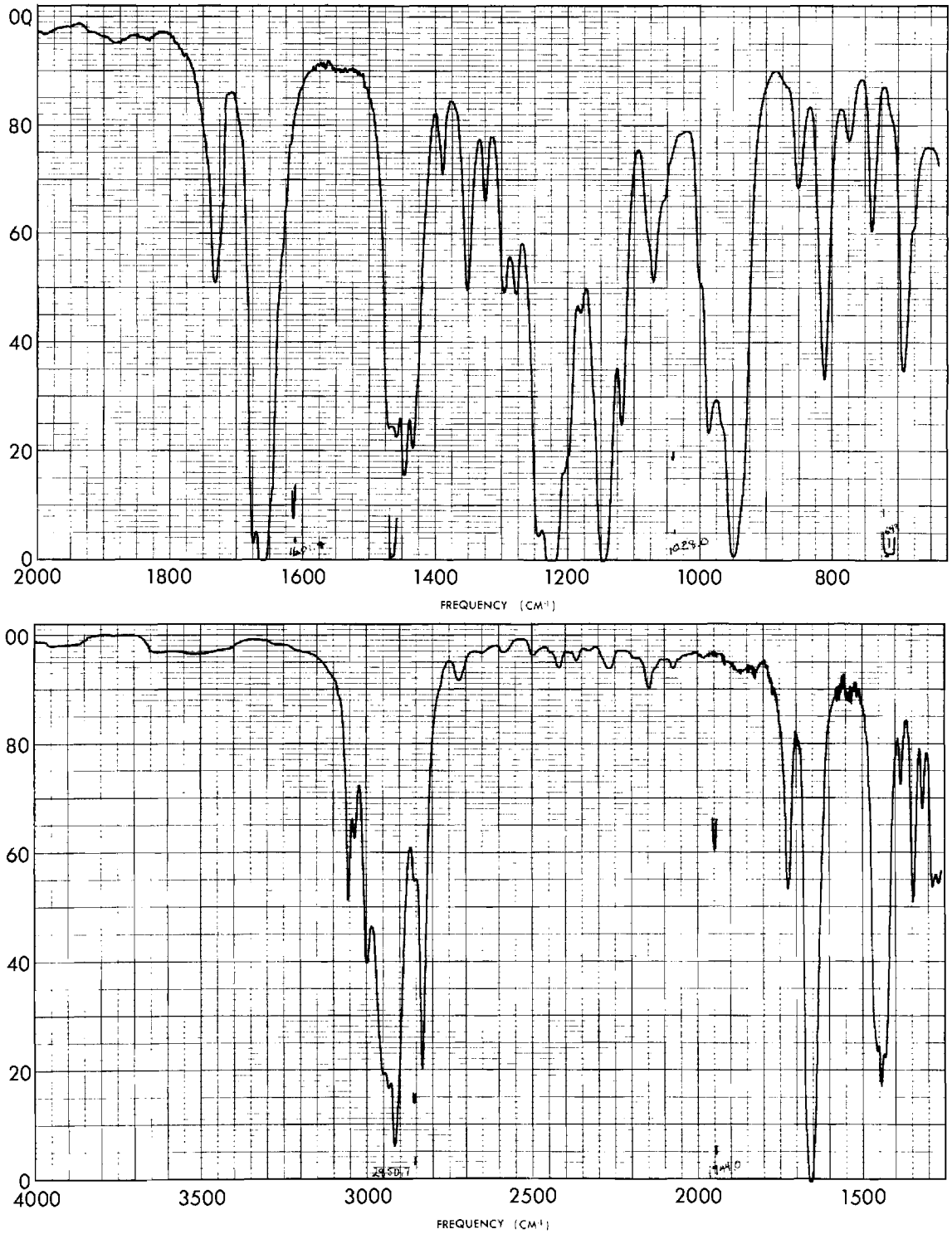

Figure 4. Infrared Spectrum of trans-1-Methoxy-3-methylthiopropene. (ca. 91 per cent trans and 9 per cent cis)

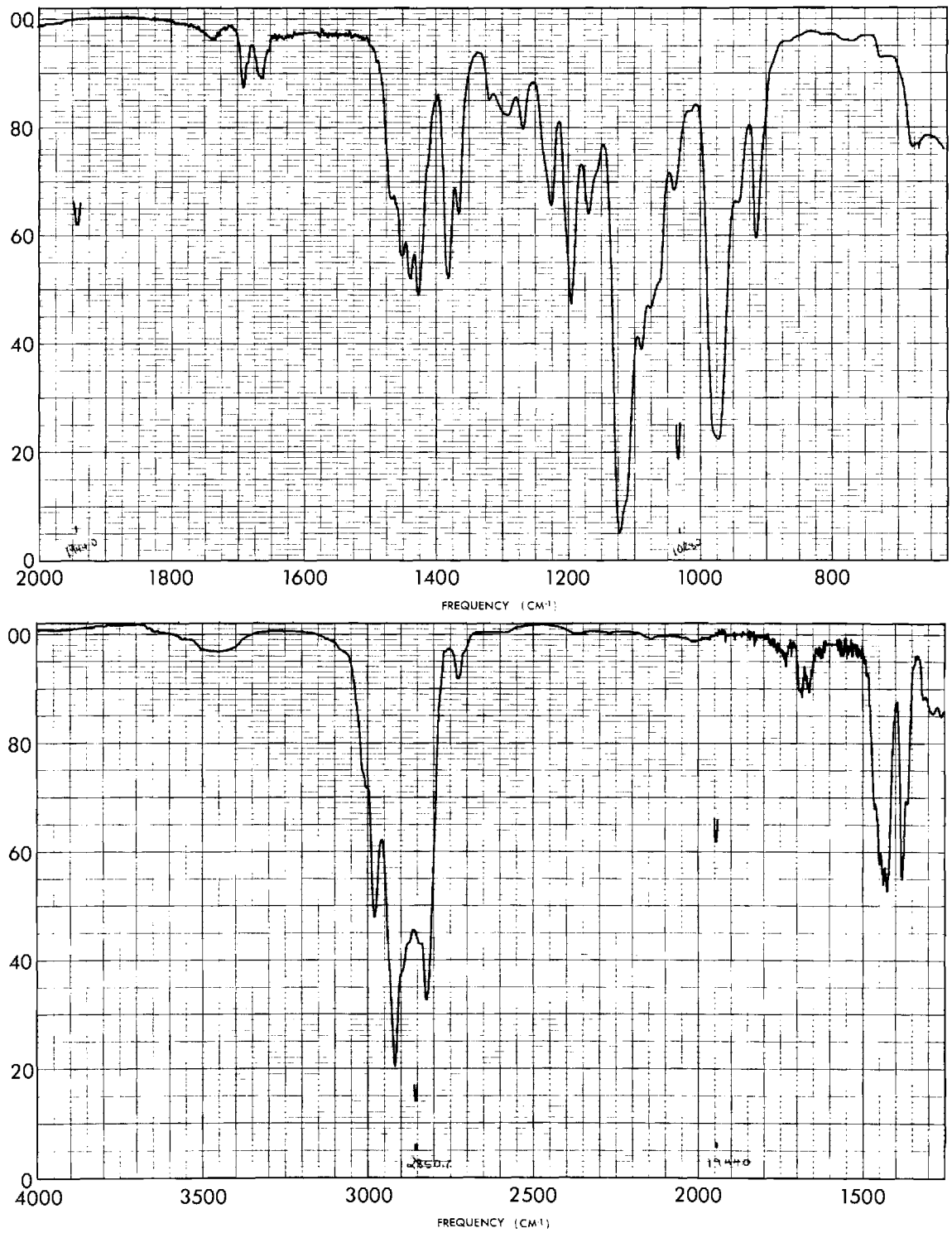

Figure 5. Infrared Spectrum of trans-1-Methoxy-4-methylthio-2-butene.

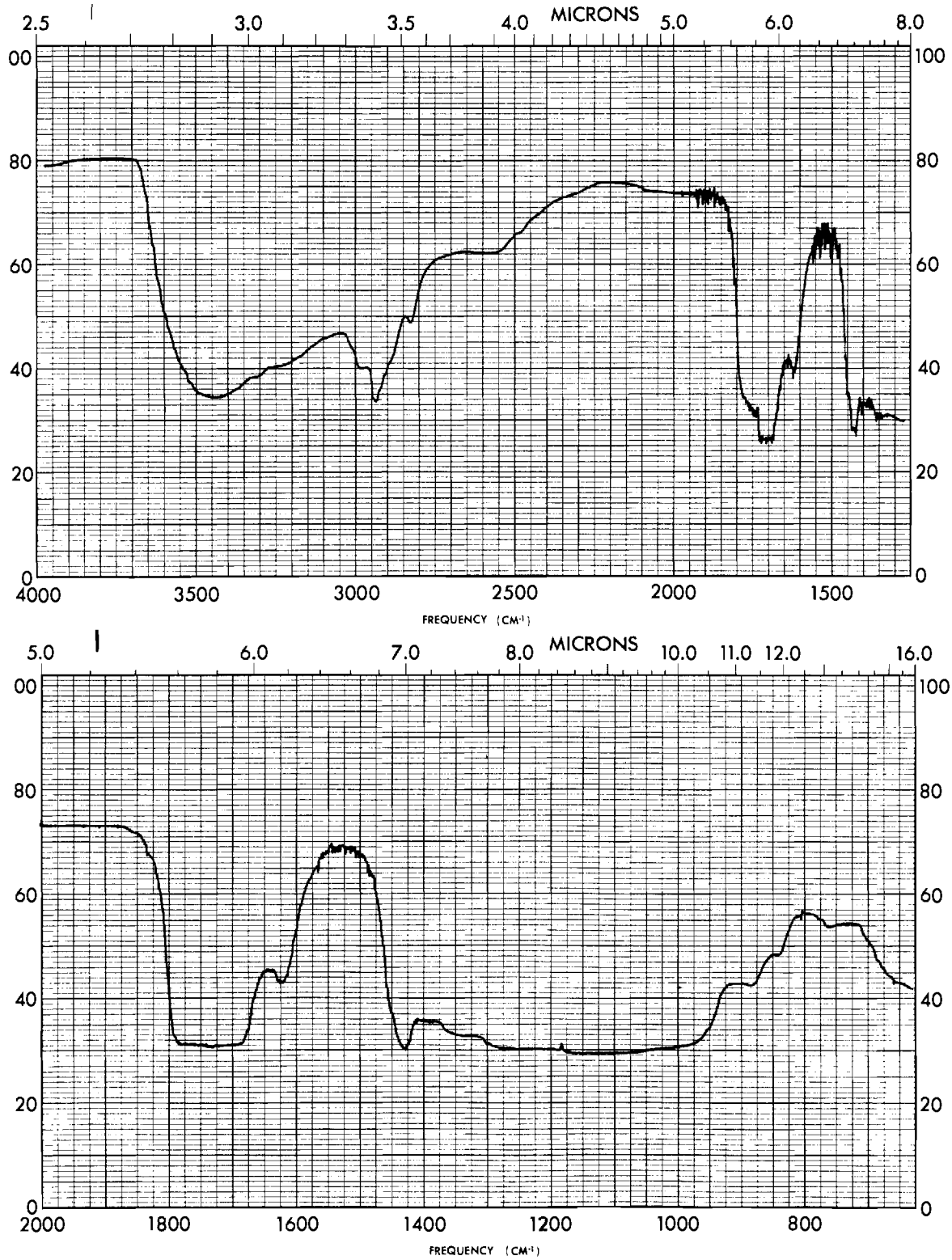

Figure 6. Infrared Spectrum of Methyl cis-4-Methoxy-3-butenoate.

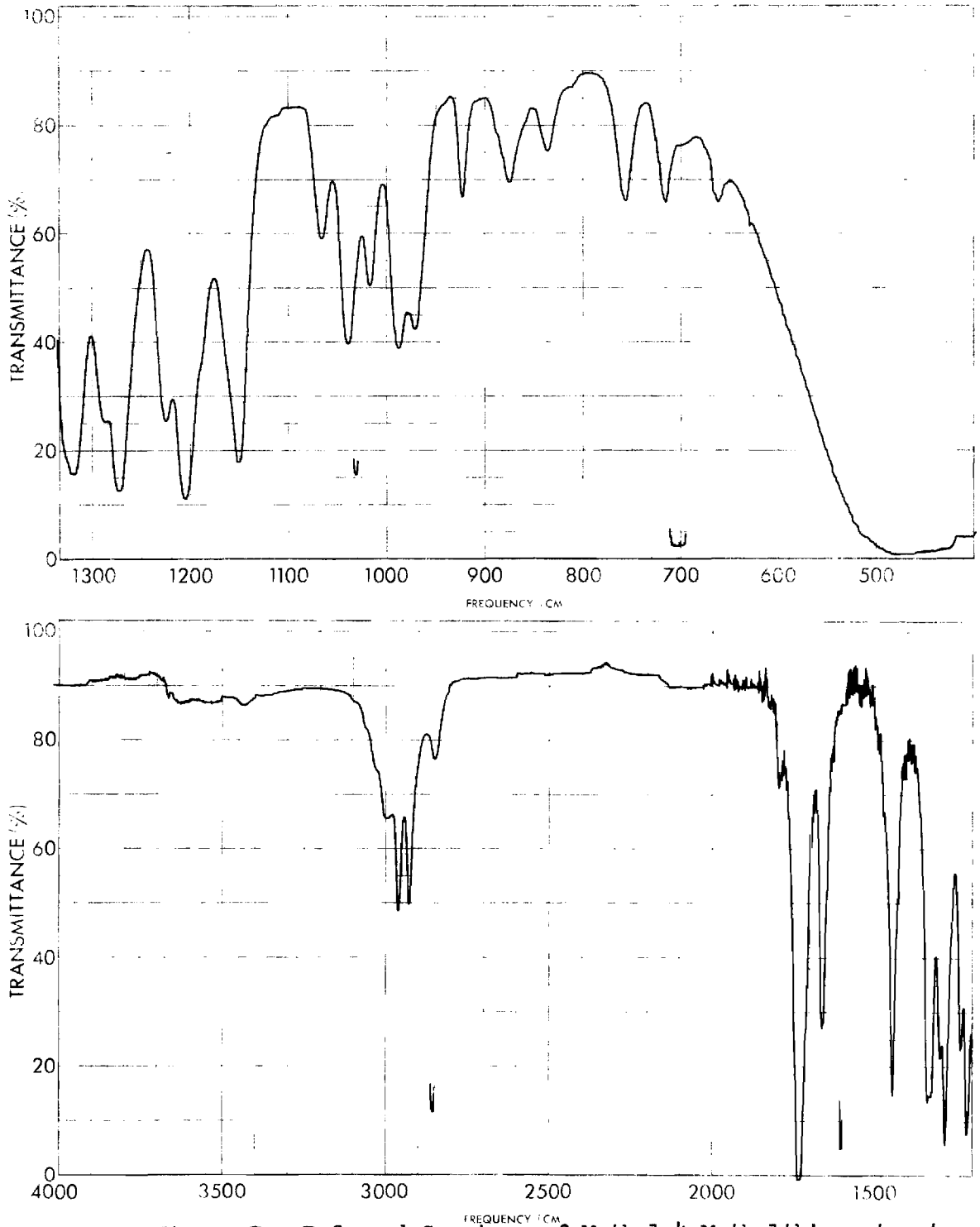

Figure 7. Infrared Spectrum of Methyl 4-Methylthiocrotonate.

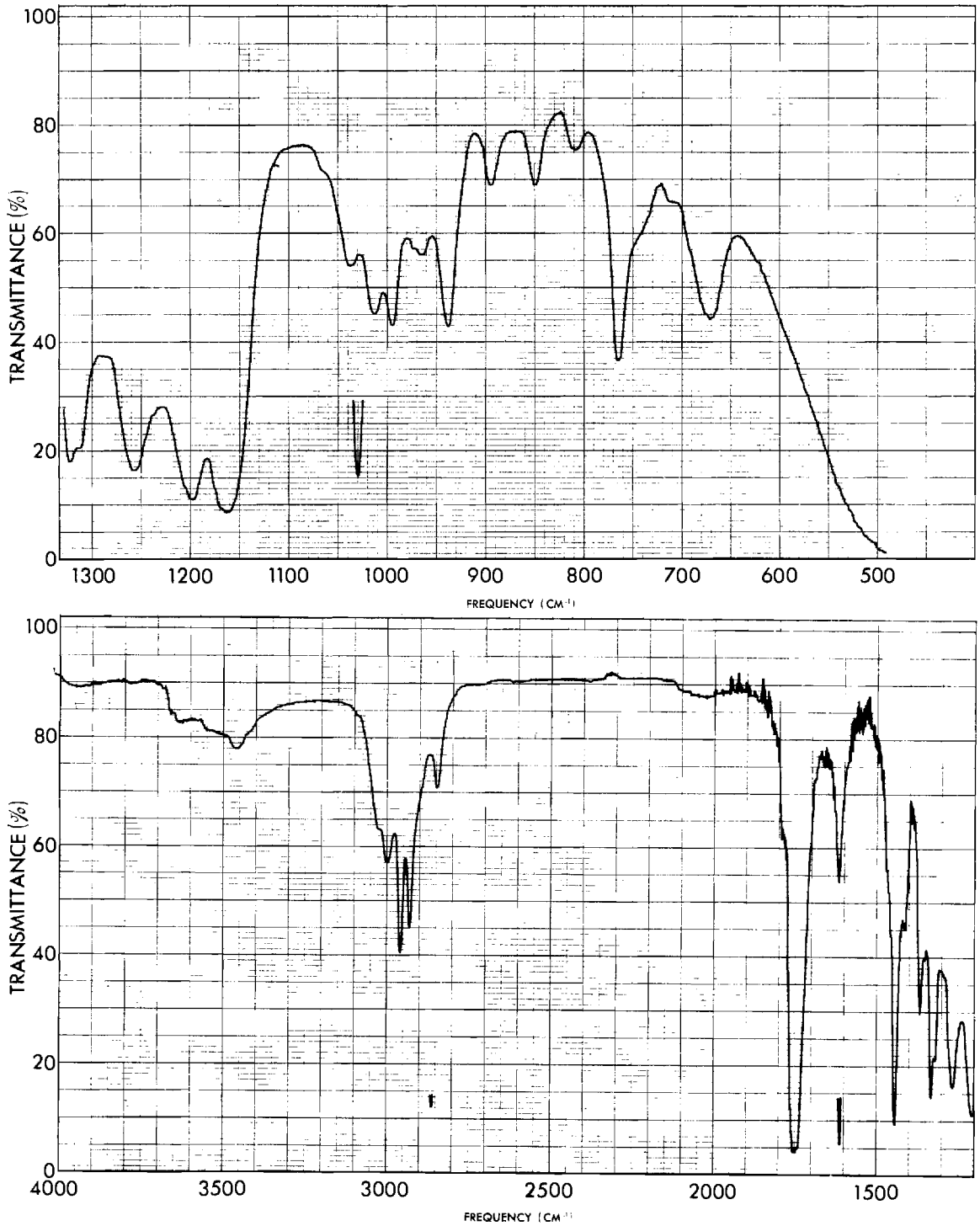

Figure 8. Infrared Spectrum of Methyl cis-4-Methylthio-3-butenoate. (ca. 95 per cent cis, ca. 3 per cent trans, and ca. 2 per cent Methyl 4-Methylthio-crotonate)

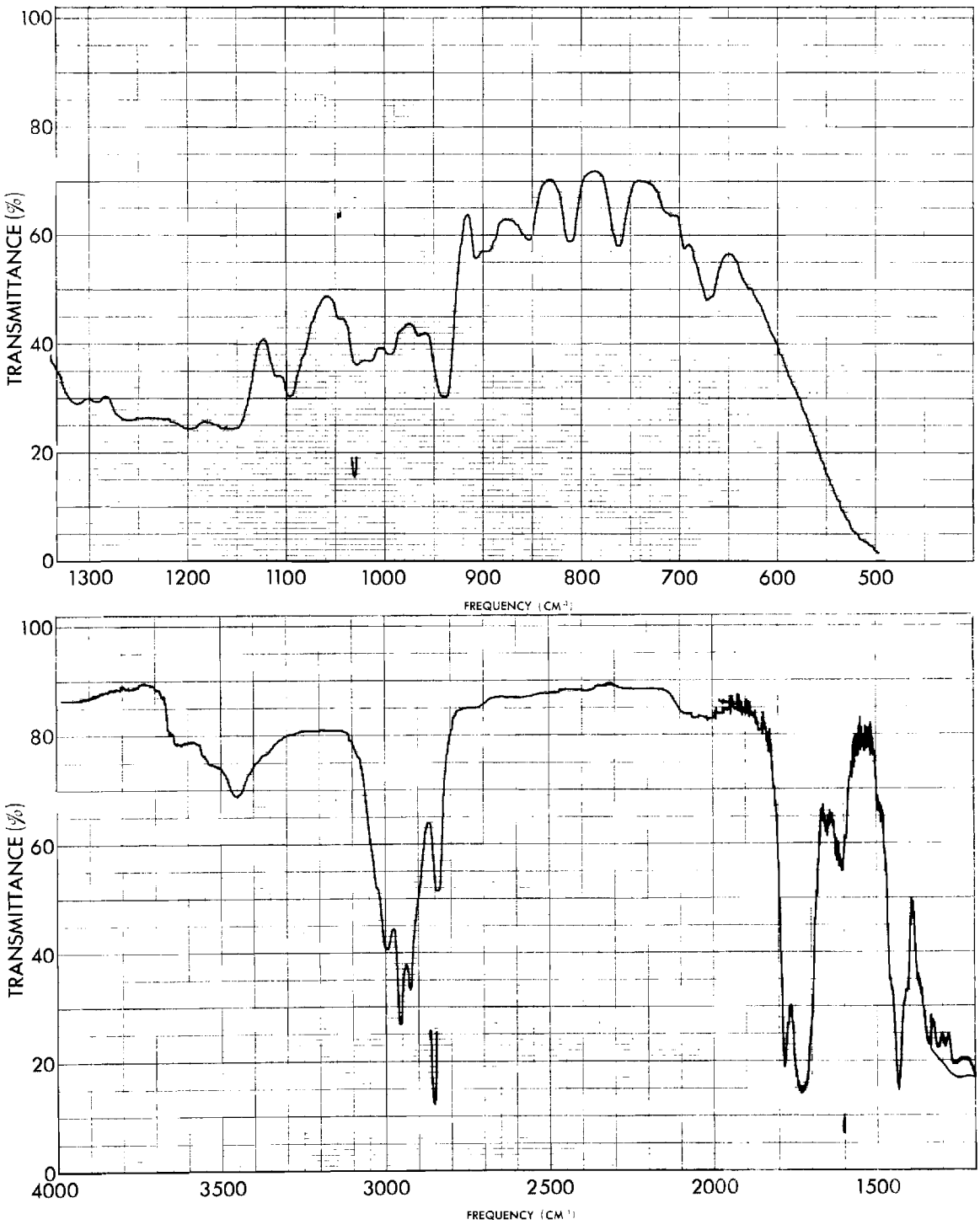

Figure 9. Infrared Spectrum of Methyl trans-4-Methylthio-3-butenoate. (ca. 80 per cent trans, ca. 10 per cent cis, and ca. 10 per cent Methyl 4-Methylthiocrotonate)

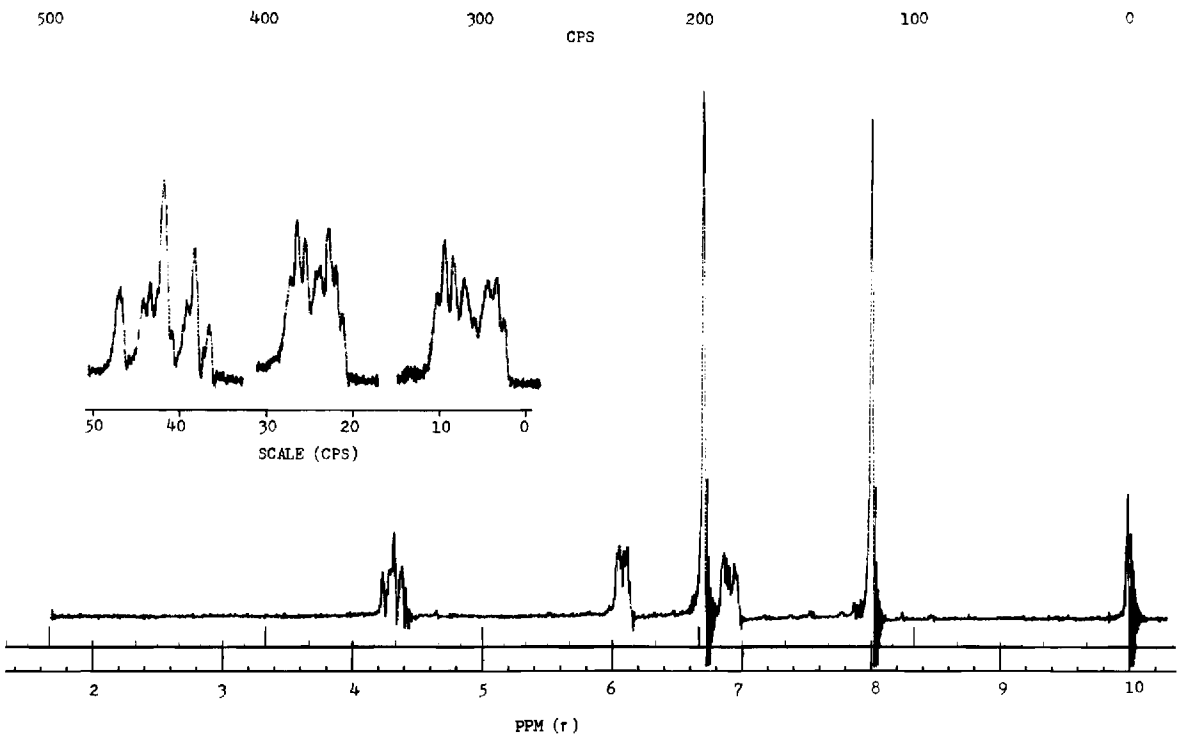

Figure 10. Nuclear Magnetic Resonance Spectrum of trans-1-Methoxy-4-methylthio-2-butene in carbon tetrachloride. Filter Bandwidth: 4 c.p.s.; R. F. Field: 0.08 mG.; Sweep Time: 500 sec.; Sweep Width: 1000 c.p.s.; Sweep Offset: 0; Spectrum Amp.: 0.08; Insert Sweep Width: 250 c.p.s.; Spectrum Amp.: 0.16.

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